[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, HARVARD UNIVERSITY]

Synthesis of 6-Methylaceanthrene[2]

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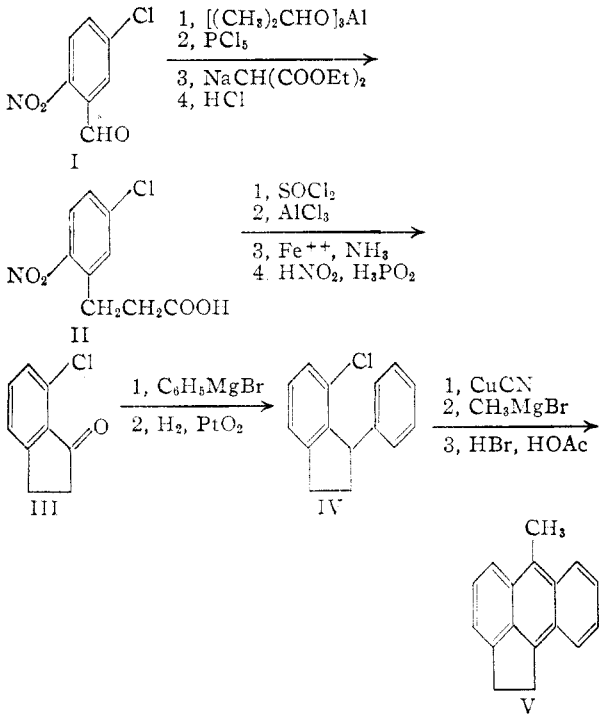
The synthesis of 6-methylaceanthrene was accomplished by starting with a derivative of *m*-chlorobenzaldehyde that contained a nitro group to block cyclization in the undesired direction. The final step was a Bradsher ring closure.

6-Methylaceanthrene[3] (V) was synthesized by the sequence of reactions outlined in the accompanying chart. The key intermediate, 7-chlorohydrindone-1 (III), prepared first by Kenner and Witham[4] by a rather elaborate synthesis, was obtained in a series of steps starting with 2-nitro-5-chlorobenzaldehyde (I). The aldehyde was reduced with aluminum isopropoxide to the benzyl alcohol, which afforded the chloride on treatment with phosphorus pentachloride in chloroform. Conversion of the chloride to the substituted malonic ester was effected by a procedure similar to that of Reissert[5] except that a larger excess of malonic ester was used in order to minimize formation of the doubly substituted ester.[6] Although the chlorine-free ester can be hydrolyzed by alkali,[5,6] attempted alkaline hydrolysis of the chlorine-containing ester resulted in formation of indigo-like blue material presumably derived from a product of cyclization. However, treatment with hydrochloric acid effected both hydrolysis and decarboxylation; the resulting hydrocinnamic acid II was cyclized through the acid chloride and afforded 4-nitro-7-chlorohydrindone-1 in 69% yield. The nitro group, originally introduced to prevent cyclization in the 2-position, was reduced and the amino group eliminated by diazotization and reduction with hypophosphorous acid. The ketone III was converted by condensation with phenylmagnesium bromide and hydrogenation to crystalline 1-phenyl-7-chlorohydrindene (IV). The corresponding 7-nitrile and 7-aceto derivatives were not obtained crystalline but were employed as oils. 6-Methylaceanthrene (V) was obtained by cyclization of the 7-aceto derivative by the general method developed by Bradsher[7]; the hydrocarbon, isolated in pure condition in only small amounts, forms yellowish needles, m.p. 158–159.5°.



Experimental[8]

2-Nitro-5-chlorobenzyl Alcohol.—2-Nitro-5-chlorobenzaldehyde was prepared from *m*-chlorobenzaldehyde[9] according to Eichengrün and Einhorn[10] in 87.5% yield; crystallization from benzene–ligroin gave long needles, m.p. 76–77°. Reduction of the aldehyde with aluminum isopropoxide afforded the benzyl alcohol in 90% yield (60–80 g. runs). The compound forms long white needles, m.p. 79.8–80.2°; a pink coloration develops on standing.

Anal. Calcd. for $C_7H_6O_3NCl$ (187.58): C, 44.82; H, 3.22. Found: C, 44.74; H, 3.13.

2-Nitro-5-chlorobenzyl chloride was prepared by dissolving the above alcohol (64 g.) in dry chloroform (400 cc.) and adding phosphorus pentachloride (72 g.) in small portions. The chloroform layer was washed with ice-cold water, dried over sodium sulfate, and evaporated. A solution of the residue in absolute ethanol was clarified with Norit, filtered, concentrated and chilled in an ice-bath. When slightly impure, the chloride has very unpleasant lachrymatory properties and is reluctant to crystallize. Crystallization is facilitated by removing the phosphorus oxychloride as well as the chloroform by evaporation in vacuum. The combined crude crystallizates from 125 g. of the alcohol weighed 120 g. (87%); recrystallization from absolute ethanol afforded 111 g. (80.5%) of pure chloride. A sample recrystallized several times formed white needles, m.p. 51.4–52.2°.

Anal. Calcd. for $C_7H_5O_2NCl_2$ (206.03): C, 40.80; H, 2.45. Found: C, 40.55; H, 2.69.

2-Nitro-5-chlorohydrocinnamic Acid (II).—In a typical run, 14 g. (0.61 mole) of sodium was dissolved in small portions in 250 cc. of absolute ethanol and 120 cc. (0.79 mole) of redistilled diethyl malonate was added. The mixture was cooled to 5° in order to minimize formation of diester and a solution of 50 g. (0.24 mole) of the substituted benzyl chloride in 350 cc. of absolute ethanol, cooled to 5°, was added not too slowly. The mixture, which deposited sodium chloride at once and turned reddish, was let stand at 0° for several hours and then neutralized with cold dilute hydrochloric acid, when it turned white. The mixture was filtered and then steam distilled to remove excess malonic ester, and the organic material was collected by ether extraction. Some diester could be caused to crystallize by rubbing the ether residue with absolute ethanol, but the diester was found to be so resistant to acid hydrolysis that its removal at this point was unnecessary. The total product was thus refluxed overnight with

(1) This work was carried out in the period 1941–1943.

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(3) Numbering according to A. M. Patterson and L. T. Capell, "The Ring Index," Reinhold Publishing Corp., New York, N. Y., 1940.

(4) J. Kenner and E. Witham, *J. Chem. Soc.*, **119**, 1452 (1921).

(5) A. Reissert, *Ber.*, **29**, 633, 639 (1896).

(6) H. Leuchs, *ibid.*, **44**, 1507 (1911); A. Jaenisch, *ibid.*, **56**, 2448 (1923).

(7) C. K. Bradsher, THIS JOURNAL, **62**, 486, 1077 (1940).

(8) All melting points are corrected. Analyses by Miss E. Werble.

(9) J. S. Buck and W. S. Ide, "Organic Syntheses," Coll. Vol. II, 1943, p. 130.

(10) A. Eichengrün and A. Einhorn, *Ann.*, **262**, 133 (1891).

340 cc. of 36% hydrochloric acid and 35 cc. of water. The mixture was diluted with water and extracted with ether and the substituted malonic acid was extracted from the ether layer with dilute ammonium hydroxide. The crude acid, obtained by dropping the ammoniacal solution into stirred, ice-cold hydrochloric acid, weighed 27.2 g. (49%); a second crop of 8.5 g. (15%) was obtained by further hydrolysis of the neutral residue; the crystalline diester remained in the ether layer. Attempts to hydrolyze the monoester with sodium, potassium or barium hydroxide failed. Crystallized from absolute ethanol, the acid formed small white needles, m.p. 95.8–96.4°.

Anal. Calcd. for $C_9H_8O_4NCl$ (229.62): C, 47.07; H, 3.51. Found: C, 46.67; H, 3.87.

4-Nitro-7-chlorohydrindone-1.[11]—Purified thionyl chloride[12] (22 g.) was added to 34.5 g. of II and, when the reaction had subsided, the mixture was heated for 20 minutes on the steam-bath and then cooled; the acid chloride crystallized but was not isolated. After addition of carbon bisulfide (200 cc.) and aluminum chloride (20 g.), the mixture was refluxed for eight hours and the solvent then evaporated. The residue was decomposed with dilute sulfuric acid and the product extracted with benzene. The extract, washed neutral with sodium carbonate solution, afforded a solid on evaporation. Crystallization from alcohol afforded 22 g. (69%) of satisfactory hydrindone; the soda extract gave 8.2 g. of uncyclized acid suitable for use in subsequent runs. The hydrindone forms small, heavy white crystals, m.p. 108.4–109.4°.

Anal. Calcd. for $C_9H_6O_3NCl$ (211.60): C, 51.08; H, 2.86. Found: C, 51.27; H, 3.13.

4-Amino-7-chlorohydrindone-1.—A mixture of 64 g. of ferrous sulfate, 200 cc. of water and 200 cc. of ammonia was heated on the steam-bath and 4 g. of the nitro compound dissolved in 300 cc. of alcohol was added all at once. Reduction occurred immediately, and heating was continued for 30 minutes. The boiling solution was filtered several times, in order to remove iron salts, and the filtrate was concentrated to a small volume. The amino compound which precipitated (2.9 g. crude product, 84.5%) was filtered and crystallized from dilute alcohol. The reaction was carried out several times on 3–5 g. lots; the average yield of pure amine was 75%, but decreased when larger amounts of starting material were used. The amine forms white needles, m.p. 157.6–158.2°.

Anal. Calcd. for C_9H_8ONCl (181.62): C, 59.51; H, 4.44. Found: C, 59.74; H, 4.24.

7-Chlorohydrindone-1 (III).—The deamination of the above amine has been described elsewhere.[13] The hydrindone forms heavy, white prisms from dilute alcohol, m.p. 94.8–95.8° (lit. 98°[4]).

Anal. Calcd. for C_9H_7OCl (166.60): C, 64.88; H, 4.24. Found: C, 64.67; H, 4.42.

1-Phenyl-7-chloroindene-1.—1-Phenyl-7-chloroindene-1 was prepared in 64.5% yield from the above ketone and phenylmagnesium bromide. The product distilled at 194–197° (15–16 mm.) as a light yellow oil. The yield of redistilled product was 58.3%.

Anal. Calcd. for $C_{15}H_{11}Cl$ (226.70): C, 79.47; H, 4.89. Found: C, 79.20; H, 5.10.

1-Phenyl-7-chlorohydrindene.—Three grams of the above olefin, dissolved in 6 cc. of glacial acetic acid, was hydrogenated in the presence of 80 mg. of Adams catalyst. The reduced compound distilled at 180–183° (17 mm.) and solidified in the receiver. It forms small, colorless prisms, m.p. 59.6–60.5°.

Anal. Calcd. for $C_{15}H_{13}Cl$ (228.71): C, 78.77; H, 5.73. Found: C, 78.95; H, 5.96.

1-Phenyl-7-cyanohydrindene.—The method was similar to that described for the preparation of α-naphthonitrile.[14] A mixture of 1.27 g. of the chloro compound, 500 mg. of cuprous cyanide and 2 cc. of pyridine was heated for 24 hours at 265° and for 2 hours at 270°. If the reaction was carried out at 225° only unreacted starting material was recovered. The mixture was poured on ice and ammonia, and the organic material was taken up in benzene. The benzene layer was washed with ammonia, dilute acid, water and salt solution and was concentrated after drying. Petroleum ether caused the precipitation of a dark impurity and the filtered solution was light orange. A small sample was sublimed *in vacuo* (2 mm., bath 180–200°) and was recovered as a heavy, orange oil. The remainder of the material was used in the next step without further purification.

Anal. Calcd. for $C_{16}H_{13}N$ (219.27): C, 87.64; H, 5.97. Found: C, 87.95; H, 5.58.

1-Phenyl-7-acetylhydrindene.—The benzene solution of the nitrile was added to a Grignard solution prepared from 500 mg. of magnesium and 3 g. of methyl iodide in ether. The mixture was refluxed overnight, when a white precipitate formed. After decomposition with ammonium chloride the organic layer was dried and the solvents evaporated. The residue was boiled with a solution of 10 cc. each of hydrochloric acid, water and acetone in order to hydrolyze any ketimide hydrochloride. The organic material was dissolved in benzene–ether. After drying, the solvents were removed completely and the remaining oil was used in the next step without further purification. A small sample was sublimed *in vacuo* and formed a yellow oil.

Anal. Calcd. for $C_{17}H_{16}O$ (236.30): C, 86.40; H, 6.83. Found: C, 86.07; H, 6.56.

6-Methylaceanthrene.—The above impure methyl ketone (500 mg.) was refluxed in a mixture of 10 cc. of glacial acetic acid, 4 cc. of hydrobromic acid and 1 cc. of water for two days. After this time the acid mixture was decanted from the semi-solid dark reaction product. The latter was taken up in benzene, and the dried benzene extract was concentrated to a small volume. One gram of picric acid in alcohol was added and, after concentration, some more alcohol. A semi-solid, black picrate (A) precipitated overnight. The filtrate on further concentration afforded a quantity of purer picrate (B). The first picrate (A) was dissolved in benzene and the benzene solution was passed through a column of alumina. Addition of alcohol to the concentrated eluate precipitated yellow-greenish crystals, which melted around 180° and contained a high melting impurity. This material was discarded. Picrate B, when treated in the same way as picrate A, afforded reddish crystals with a blue fluorescence in solution. These were recrystallized three times from alcohol–benzene when the melting point remained constant at 158–159.5°. The analytical sample (29 mg.) formed small needles with a slight reddish impurity which did not affect the analysis. The combined mother liquors were treated with charcoal, which removed the reddish impurity and afforded the product as light, yellow needles of the same melting point.

Anal. Calcd. for $C_{17}H_{14}$ (218.28): C, 93.54; H, 6.46. Found: C, 93.12; H, 6.44.

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(11) For a similar cyclization see H. Hoyer, *J. prakt. Chem.*, **139**, 94 (1934).

(12) L. F. Fieser, "Experiments in Organic Chemistry," 2nd Ed., D. C. Heath and Co., Boston, Mass., 1941, p. 381.

(13) "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 295.

(14) M. S. Newman, *Org. Syntheses*, **21**, 89 (1941).