

Hard, compact glistening aggregates of plates, m. p. 152.5–153°, were formed.

Anal. Calcd. for $C_{22}H_{20}O_2NCl_2$: C, 65.0; H, 6.21. Found: C, 64.99; H, 6.42.

10-Methyl-decalone-2 (X).—220 mg. of 10-dichloromethyl-2-hydroxy-decahydronaphthalene was dissolved in 20 cc. of 10% methanolic potassium hydroxide, 0.5 g. of palladinized barium sulfate added, and the reaction mixture shaken with hydrogen for six hours at 29° and 759 mm. At the end of this time 42 cc. (1.9 mols) of hydrogen had been taken up. The reaction mixture was then poured into 60 cc. of water and extracted exhaustively with ether (6 hand extractions). The combined ethereal extracts were dried over sodium sulfate, the ether was removed, and the residual colorless viscous oil allowed to stand in the vacuum desiccator over phosphorus pentoxide. Since it did not crystallize on standing overnight, it was dissolved in 5 cc. of glacial acetic acid and oxidized directly by dropping in slowly a solution of 100 mg. of chromic oxide in 4 cc. of glacial acetic acid and 1 cc. of water. After stirring for four hours, the reaction mixture was poured into water, extracted exhaustively with ether,

and the combined ethereal extracts dried over anhydrous sodium sulfate. The residual oil obtained on evaporating the ether was converted into the 2,4-dinitrophenylhydrazone in the usual manner, pale yellow needles from methyl alcohol, m. p. 151–152°, mixed with an authentic sample prepared by Robinson's method, m. p. 151–152°. On hydrolyzing this derivative with 5% sulfuric acid and working up in the usual manner, 100 mg. of a colorless oil of camphoraceous odor was obtained which solidified on standing, m. p. 46°, mixed with Robinson's ketone, m. p. 45–46°.

Summary

A novel method for the direct introduction of the angular-methyl group is described. These experiments may be considered as models for the transformation of oestrone or oestradiol into substances of the testosterone-androsterone group.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

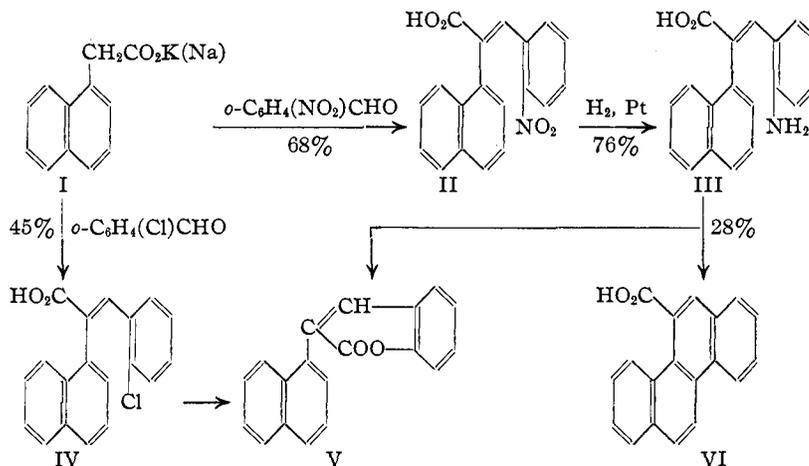
5-Methylchrysene

BY LOUIS F. FIESER AND LLOYD M. JOSHEL¹

In a previous attempt to synthesize 5-methylchrysene a rearrangement was encountered in a final dehydrogenation step and the product, isolated in small yield, proved to be the 6-methyl isomer.² Another route not requiring a dehydrogenation now has been investigated, the plan being to obtain the 5-methyl compound from the corresponding carboxylic acid.

One scheme for obtaining the desired intermediate consisted in the condensation of α -naphthylacetic acid with *o*-chlorobenzaldehyde and fusion of the product IV with potassium hydroxide, following the synthetic method employed by Hewett.³ The only crystalline product isolated proved to be the lactone of α -(1-naphthyl)-*o*-hydroxycinnamic acid, V. We then turned to the Pschorr synthesis, which already has been carried to the stage of the 5-acid

VI by Weitzenböck and Lieb.⁴ The condensation product II was obtained in improved yield and was conveniently reduced to the amine III by catalytic hydrogenation. Weitzenböck and Lieb state that the Pschorr ring closure afforded in about 20%



yield a crude product which was purified with difficulty. A number of variations were tried in the present work and the best result was a 28% yield of pure chryseno-5-carboxylic acid by a procedure

(1) Fellow of the Finney-Howell Research Foundation.

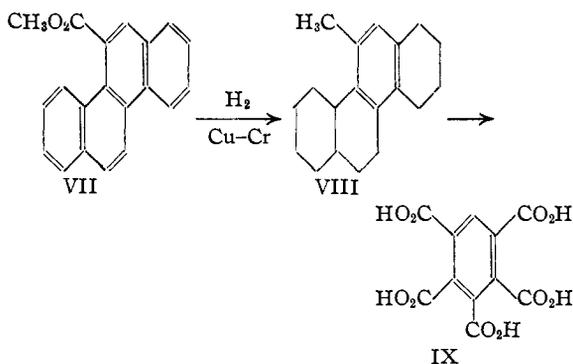
(2) Fieser, Joshel and Seligman, *THIS JOURNAL*, **61**, 2134 (1939).

(3) Hewett, *J. Chem. Soc.*, 1286 (1938).

(4) Weitzenböck and Lieb, *Monatsh.*, **88**, 549 (1912).

using copper bronze and sodium hypophosphite.⁵ A neutral by-product of the reaction had the composition of the lactone V.

On attempting to obtain either the 5-methyl or 5-hydroxymethyl compound by the direct reduction of the 5-carbomethoxy derivative VII it became apparent that the nucleus is reduced about as easily as the ester group. Reduction with sodium and ethanol gave a non-crystalline product having approximately eight hydrogen atoms more than the expected carbinol. The only crystalline reaction product isolated in various attempted hydrogenations over copper chromite catalyst was obtained on conducting the reaction at 250° for seventeen hours and proved to be 5-methyl-1,2,3,4,7,8,9,10,11,12,13,14-dodecahydrochrysene (VIII), for it gave benzene-pentacarboxylic acid (IX) on oxidation with dilute nitric acid.



With a shorter reaction period the product was a glass having approximately the composition of an octahydride. On attempting to prevent overhydrogenation at 250° by using a nitrogen-hydrogen mixture containing just the required amount of the latter gas⁶ we recovered the ester unchanged. Hydrogenation in the usual way at 160° gave a glassy mixture having the composition of a dihydro derivative of the ester VII.

The preparation of the desired 5-methyl derivative was accomplished satisfactorily by converting the acid VI by the Sonn and Müller reaction to the aldehyde, which was isolated as the semicarbazone, and reducing this by the Wolff-Kishner method. The hydrocarbon, m. p. 116.8–117.6°, proved identical with the 5-methylchrysene synthesized by Dr. M. S. Newman by a different method.⁷

(5) Ruggli and Staub, *Helv. Chim. Acta*, **20**, 37 (1937).

(6) Durland and Adkins, *This Journal*, **60**, 1501 (1938); Stutzman and Adkins, *ibid.*, **61**, 3303 (1939).

(7) Private communication, and *ibid.*, **62**, 870 (1940).

Experimental Part⁸

α -(1-Naphthyl)-*o*-chlorocinnamic Acid (IV).—A mixture of 6.4 g. of the sodium salt of α -naphthylacetic acid, 4.5 g. of freshly distilled *o*-chlorobenzaldehyde, and 50 cc. of acetic anhydride was heated in a bath at 135° for twenty-five hours and poured into water. After standing overnight the orange-yellow resin was separated by decantation and extracted with boiling aqueous potassium carbonate. After clarification with Norit and cooling the potassium salt of IV separated as colorless plates (washed with potassium carbonate solution). From the filtrate, by acidification and crystallization of the precipitate from benzene, there was obtained 1 g. of *o*-chlorocinnamic acid, m. p. 209–211°. The acid liberated from the potassium salt on crystallization from benzene-ligroin was obtained as colorless prisms which partially melted at 160°, solidified, and remelted at 171–172.5°; yield 4.3 g. (45%). The behavior on melting was not altered by recrystallization as such or as the potassium salt.

*Anal.*⁹ Calcd. for C₁₅H₁₃O₂Cl: Cl, 11.48. Found: Cl, 11.29.

In a typical attempted cyclization 4.5 g. of the chloro acid IV was fused with 25 g. of potassium hydroxide at 200–235° for five minutes and the temperature was raised to 245° in ten minutes. The crude acidic material was refluxed overnight with alcoholic hydrogen chloride and the neutral fraction separated and distilled in vacuum. The glassy distillate yielded no crystalline trinitrobenzene derivative, but after saponification and acidification a crystalline product was obtained from benzene-ligroin. This formed needles, m. p. 241–243°, dec., amounting to 0.15 g. (4%). On recrystallization the substance formed light buff needles, m. p. 244–245°, and did not depress the m. p. of the sample of the lactone V obtained as a by-product in the Pschorr synthesis.

α -(1-Naphthyl)-*o*-nitrocinnamic Acid (II).—The potassium salt of α -naphthylacetic acid was prepared by exactly neutralizing the acid in methanol with methyl alcoholic potassium hydroxide and evaporating to dryness. A solution of 25 g. of the salt and 20 g. of *o*-nitrobenzaldehyde in 200 cc. of acetic anhydride was heated in a bath at 125–130° for one hour and poured into excess dilute hydrochloric acid. After standing overnight the aqueous layer was decanted and the residue extracted with boiling potassium carbonate solution. The clarified filtrate when treated with more potassium carbonate and cooled deposited the salt of II in glistening plates. The alkaline mother liquor afforded 2.5 g. of *o*-nitrocinnamic acid, m. p. 245–247° (from acetone). The acid liberated from the salt crystallized from benzene-ligroin as yellow prisms, m. p. 181–182°; yield 24.2 g. (68%). A recrystallized sample melted at 181.8–182.8°.

Weitzenböck and Lieb⁴ obtained a product, m. p. 173–174°, in 40% yield after a reaction period of eight to nine hours. In the present work it was found advantageous to shorten the period of heating and to separate the two acidic products through the salts rather than by crystallization as such.

(8) All melting points are corrected. Microanalyses by Lyon Southworth except as noted.

(9) Analysis by Herbert S. Wight.

α -(1-Naphthyl)-*o*-aminocinnamic Acid (III).—While the nitro compound II can be reduced in good yield on a small scale with ferrous sulfate,⁴ hydrogenation seemed more satisfactory with larger amounts. With 32 g. of acid in 250 cc. of absolute ethanol and 0.2 g. of Adams catalyst, 90% of the theoretical amount of hydrogen was absorbed in two hours and the reaction then stopped. On two crystallizations from dilute alcohol the amino acid formed silvery white plates, m. p. 175–176°; yield 22 g. (76%).

Chrysene-5-carboxylic Acid (VI).—A solution of 4.5 g. of the amino acid III in 175 cc. of alcohol was treated with 1.8 cc. of concentrated sulfuric acid, followed by 3.6 cc. of amyl nitrite. After being stirred at room temperature for one-half hour the deep orange solution was added from a dropping funnel during forty-five minutes to a stirred suspension of 0.2 g. of copper bronze in 15 cc. of water and 15 g. of sodium hypophosphite at 45–50°. A test for diazonium salt with β -naphthol was negative within five minutes after the addition. The mixture was poured into excess potassium carbonate solution, the alcohol was distilled, and the hot solution was clarified with Norit and acidified. The light brown, granular precipitate was dried and allowed to stand in solution in 100 cc. of 3–5% methyl alcoholic hydrogen chloride for twelve hours. The solution was diluted with water, extracted with ether, and the acid VI, which is not esterified under these conditions, was extracted with aqueous sodium carbonate solution. The carbonate extract was clarified with Norit and the liberated acid crystallized twice from acetone–benzene, furnishing 1.2 g. (28%) of satisfactory product as buff needles, m. p. 225–226°, dec.

The neutral fraction was distilled in vacuum and crystallized three times from acetone–benzene, yielding 0.1–0.2 g. of yellow needles, m. p. 244.5–245.5°, dec., having the composition of the lactone of α -(1-naphthyl)-*o*-hydroxycinnamic acid (V).

Anal. Calcd. for $C_{19}H_{12}O_2$: C, 83.80; H, 4.44. Found: C, 83.59; H, 4.42.

As solvent in the Pschorr reaction dioxane¹⁰ or acetic acid proved less satisfactory.

Methyl 5-chrysene carboxylate was prepared from 2.5 g. of the acid in 50 cc. of acetone, treated with an ethereal solution of diazomethane from 5 cc. of nitrosomethylurethan. On distillation in vacuum and crystallization from benzene the ester formed colorless prisms, m. p. 159–160° (90% yield).

Anal. Calcd. for $C_{20}H_{14}O_2$: C, 83.89; H, 4.93. Found: C, 83.85; H, 5.04.

Bouveault Reduction.—After treatment in benzene with the calculated amount of ethanol and sodium, the ester was largely recovered unchanged. In another experiment 0.4 g. of powdered sodium was added in two portions to 0.3 g. of the ester in 5 cc. of benzene and 20 cc. of absolute ethanol and the mixture was refluxed for a few minutes, when all the sodium had reacted. After dilution, acidification and removal of the solvents with steam, the product was distilled in vacuum. A small amount (10 mg.) of the starting ester crystallized from the distillate and the main product was a light yellow glass probably consisting mainly

of 5-hydroxymethyloctahydrochrysene (calcd. for $C_{18}H_{22}O$: C, 85.67; H, 8.33. Found: C, 84.99; H, 7.77).

5-Methyl-1,2,3,4,7,8,9,10,11,12,13,14-dodecahydrochrysene (VIII).—Hydrogenation of 1 g. of the ester in 8 cc. of dioxane with 0.1 g. of copper-chromite catalyst 37KAF was conducted at 250° and 2100 lb. (140 atm.) pressure for seventeen hours. Distillation in vacuum and crystallization from benzene–alcohol furnished 0.52 g. (58.5%) of colorless needles, m. p. 95–99°. On recrystallization the hydrocarbon melted at 98.8–99.8° (0.35 g.).

Anal. Calcd. for $C_{19}H_{26}$: C, 89.70; H, 10.30. Found: C, 89.90; H, 10.56.

For oxidation 0.3 g. of the hydrocarbon was heated with 1.5 cc. of concentrated nitric acid and 3 cc. of water at 195–200° for twenty-two hours. The clear yellow solution was taken to dryness and the residue allowed to stand for several hours with diazomethane solution. After sublimation of the ester at 2 mm. pressure, crystallization from ether–ligroin gave 0.05 g. of prisms and after recrystallization the sample of pentacarbomethoxybenzene melted at 146–149.5°.

Anal. Calcd. for $C_{16}H_{16}O_{10}$: C, 52.18; H, 4.38. Found: C, 52.28; H, 4.73.

Pentacarbomethoxybenzene is described as melting at 150.5° with previous sintering.¹¹ The ester of prehnitic acid (1,2,3,4), which would be the expected product if the alternate non-terminal ring were aromatic, melts at 131–133°.

Other Hydrogenations.—On hydrogenation of the ester as above but for only four hours there was obtained a small amount of the crystalline dodecahydride and a colorless glass of composition corresponding approximately to an octahydride (calcd. for $C_{13}H_{22}$: C, 91.15; H, 8.85. Found: C, 90.50; H, 8.35). On conducting the reaction at 160° for four hours the non-crystalline product corresponded most closely to a dihydro ester (calcd. for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 83.10; H, 5.83).

Chrysene-5-aldehyde Semicarbazone.—A mixture of 0.56 g. of chrysene-5-carboxylic acid, 0.5 cc. of phosphorus pentachloride, and 10 cc. of benzene was refluxed for ten minutes and the resulting solution was evaporated to dryness at reduced pressure. The residue was taken into 15 cc. of dry acetone and treated with 2 cc. of aniline, and after boiling for a few minutes the anilide which separated was collected, washed with benzene, and heated with 0.5 g. of phosphorus pentachloride in 5 cc. of benzene for one-half hour. Evaporation in vacuum left the chloroanilide as a bright red oil. This was dissolved in 5 cc. of ethylene chloride and added to a solution prepared by passing hydrogen chloride into 1.5 g. of anhydrous stannous chloride suspended in 15 cc. of dry ether. After sixteen hours at 0°, 15 cc. of water was added and the mixture refluxed for two hours and steam distilled. The residue was extracted with benzene, the solvent was replaced by absolute alcohol, 5 cc. of pyridine and 0.3 g. of semicarbazide hydrochloride were added and the solution was refluxed for one hour and diluted with water. The semicarbazone crystallized as light yellow microprisms, m. p. 260–263°, dec.; yield 0.34 g. (53%). Recrystallized from acetic acid, the substance melted at 266–268°, dec.

(10) Cassaday and Bogert, *This Journal*, **61**, 2461, 3055, 3058 (1939).

(11) Späth, Wessely and Kornfeld, *Ber.*, **65**, 1549 (1932).

Anal. Calcd. for $C_{20}H_{16}ON_3$: N, 13.41. Found: N, 13.21.

5-Methylchrysene.—The semicarbazone (0.23 g.) was heated with a solution from 0.3 g. of sodium and 10 cc. of absolute alcohol in a sealed tube at 200° for nine hours. After dilution and acidification the product was extracted with benzene and the washed and dried solution was passed through a tower of alumina. After vacuum distillation the product was fractionally crystallized from alcohol to remove a small amount of chrysene. The 5-methyl compound then crystallized from alcohol in colorless needles, m. p. 116.8 – 117.6° ; yield 0.03 g. (17%).

Anal. Calcd. for $C_{19}H_{14}$: C, 94.18; H, 5.82. Found: C, 94.35; H, 5.61.

The hydrocarbon shows strong blue-violet fluorescence in ultraviolet light. The substance did not depress the m. p. of a sample kindly supplied by Dr. M. S. Newman.

The picrate formed red needles, m. p. 141.6 – 142.4° , from alcohol.

Anal. Calcd. for $C_{25}H_{17}O_7N_3$: N, 8.91. Found: N, 8.80.

Summary

Chrysene-5-carboxylic acid, obtained by the Pschorr synthesis, has been converted through the aldehyde (Sonn-Müller reaction) to the 5-methyl compound. In attempts to reduce the ester with sodium and ethanol or by high pressure hydrogenation, the aromatic nucleus was invariably attacked.

CONVERSE MEMORIAL LABORATORY

CAMBRIDGE, MASSACHUSETTS RECEIVED MARCH 12, 1940

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Oxidation Products of Sulfanilamide

BY MARGARET K. SEIKEL¹

Sulfanilamide (I) oxidizes with ordinary oxidizing agents either to azobenzene-4,4'-disulfonamide (II) or to azoxybenzene-4,4'-disulfonamide (III). Both II and III can be reduced to I and to hydrazobenzene-4,4'-disulfonamide (IV).² Oxidation of sulfanilamide with cold alkaline ferricyanide produced a 20% yield of the azo compound II.³ A better method for preparing II, with the over-all yield of brighter colored product as high as 46%, comprises the series of reactions $I \rightarrow III \rightarrow IV \rightarrow II$. II could be converted into III by heating for several hours with hydrogen peroxide in glacial acetic acid.⁴

When I was oxidized in glacial acetic acid with 30% hydrogen peroxide, the azoxy compound III was obtained in 70% yields after only half an hour's heating. The speed with which III was obtained from I in comparison with the slow conversion of II to III indicated that II is probably not an intermediate in the former reaction; likewise IV yielded mainly II by the same treatment.⁵ However, with this reagent *p*-toluidine is oxidized first to the corresponding azo

compound so undoubtedly the sulfonamido group affects the course of the reaction.

If I was oxidized by hydrogen peroxide in dilute sulfuric acid, the product was a mixture of II and III. If hydrochloric acid was employed as the acidifying agent, partial chlorination yielded mixtures of products. Oxidations by hydrogen peroxide in neutral or basic solutions were too slow to be practical.

Reductions of II, III or material believed to be a mixture of the two by stannous chloride in hydrochloric acid regenerated sulfanilamide in 35–50% yields.^{3a} Reductions with hydrosulfite in alkaline solution produced quantitative yields of IV.

Reoxidation of IV to II occurred very readily with various oxidizing agents, but 1 *N* ferric chloride was preferable because it yielded instantaneous and quantitative results.

Sulfanilamide may be chlorinated in the cold by treatment with a great excess of hydrochloric acid and only a moderate excess of hydrogen peroxide, the previously unreported 3,5-dichloro-4-amino-benzenesulfonamide (V) separating in fair yields. The reaction undoubtedly occurs through an intermediate chloramide.

Experimental

All melting points are uncorrected and were taken by the method described in Mulliken's "Identification of

(1) Research Associate.

(2) For biological tests on II, III and IV see *Compt. rend.*, **205**, 181 (1937).

(3) (a) Laar, *Ber.*, **14**, 1928–1934 (1881); (b) Limpricht, *ibid.*, 1356–1359; (c) Scudi, *This Journal*, **59**, 1480–1483 (1937). No melting point is recorded.

(4) Compare Angeli, *Chem. Zentr.*, **81**, II, 731 (1910).

(5) Compare D'Ans and Kneip, *Ber.*, **48**, 1145 (1915).