

the theoretical required for one double bond. Under conditions of alkaline hypoiodite oxidation¹⁰ 200 mg. of the substance consumed 18.4 cc. of 0.1 molar (I₂) iodine solution; calculated for four atoms of iodine per mole of tetramethylglucoseen, 18.3 cc. This iodine consumption is equivalent to an "apparent tetramethylaldehyde value"¹⁰ of 217%.

(10) F. A. Cajori, *J. Biol. Chem.*, **54**, 617 (1922); cf. ref. 6.

Summary

1. 1-Diethylamino-2,3,4,6-tetramethyl-*d*-glucose and 2,3,4,6-tetramethyl-1,2-*d*-glucoseen have been synthesized in crystalline condition. Some of the properties of the latter compound have been noted.

COLUMBUS, OHIO

RECEIVED OCTOBER 16, 1937

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

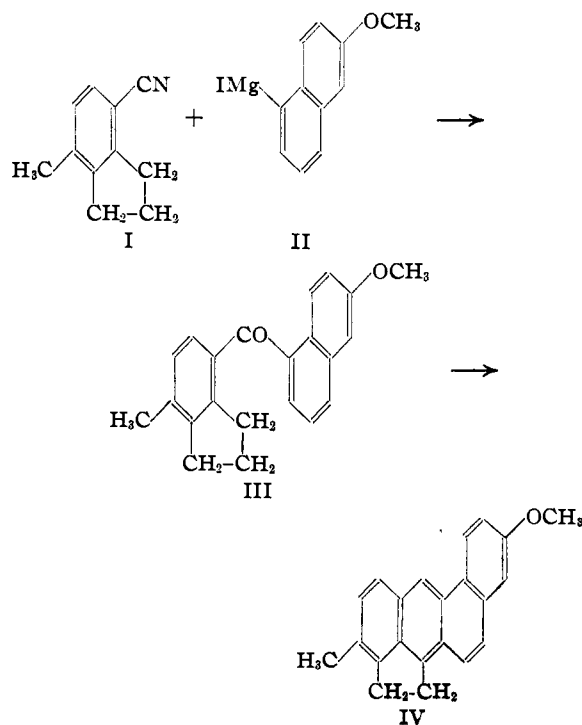
The Synthesis of 3-Substituted Derivatives of Methylcholanthrene

BY LOUIS F. FIESER AND BYRON RIEGEL¹

This investigation was undertaken to determine whether the cholanthrene synthesis of Fieser and Seligman² can be employed for the preparation of cholanthrene derivatives containing substituents other than alkyl groups, and, in case such compounds should be found to withstand the rather drastic pyrolysis involved in the final step, to synthesize by this method certain 3-substituted methylcholanthrenes (sterol numbering system^{2b}). We were particularly interested in the 3-hydroxy compound, since this conceivably may arise in the organism as a product of steroid metabolism, but we temporarily discontinued our work in this direction at an early stage because of the appearance in the autumn of 1936 of a paper containing an announcement of the synthesis of 3-hydroxymethylcholanthrene by Cook and de Worms.³ No information concerning the method of synthesis or the physical properties of the compound was included either in this announcement or in subsequent discussions of the compound in other publications⁴ from the Royal Cancer Hospital and, since our plan of synthesis involved the application of a general method discovered and actively investigated in this Laboratory, we eventually decided to complete our work in order to provide for bioassays a sample of the compound obtained by a synthesis presumably different from that employed by the

London group. On communicating our results to Professor Cook in advance of publication, however, we learned that he and de Worms had used the same method, except for a minor variation in an intermediate step. Following Professor Cook's suggestion that the results from the two Laboratories be published simultaneously, we are recording herewith our own observations, but in doing so we cordially acknowledge the priority of the English investigators.

In our synthesis the previously described 4-methyl-7-cyanohydrindene^{2d} (I) was first condensed with the Grignard reagent (II) from 6-methoxy-1-iodonaphthalene, prepared from



(1) National Research Fellow in Medicine.

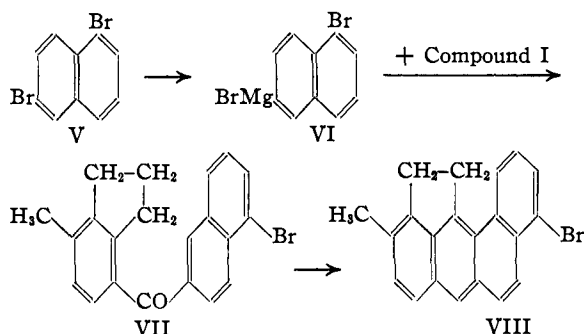
(2) (a) Fieser and Seligman, *THIS JOURNAL*, **57**, 942 (1935); (b) **57**, 1377 (1935); (c) **57**, 2174 (1935); (d) **58**, 2482 (1936); (e) **59**, 883 (1937); (f) Fieser and Hershberg, *ibid.*, **57**, 1681 (1935); (g) **59**, 394 (1937); (h) Bruce with Fieser, *ibid.*, **59**, 479 (1937).

(3) Cook, Haslewood, Hewett, Hieger, Kennaway and Mayneord, Reports of the II International Congress of Scientific and Social Campaign against Cancer, **1**, 1 (1936).

(4) (a) *Idem*, *Am. J. Cancer*, **29**, 219 (1937); (b) Cook, *Bull. soc. chim.*, [5] **4**, 792 (1937); (c) Bachmann, Cook, Dansi, de Worms, Haslewood, Hewett and Robinson, *Proc. Roy. Soc. (London)*, **129B**, 843 (1937).

Cleve's acid according to Butenandt and Schramm.⁵ The resulting ketone, III, underwent rapid cyclodehydration when heated with zinc dust at 405° and the methoxy compound IV was obtained in 38% yield. Acid hydrolysis gave 3-hydroxy-20-methylcholanthrene, m. p. 220.5–222°, corr.

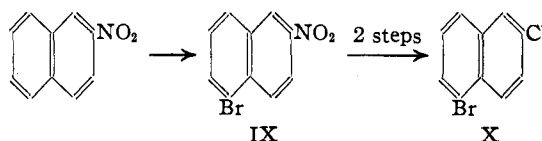
The application of this scheme of synthesis is limited chiefly by the difficulty of obtaining 6-substituted 1-naphthyl halides for use as starting materials. We first considered the possibility of using the comparatively readily available 1,6-dibromonaphthalene (V), for from the usual relationship in the naphthalene series the bromine atom in the α -position would be expected to enter into reaction with magnesium in preference to that in the β -position 6. Salkind,⁶ however, reports that a preliminary experiment indicated that the reaction probably follows the alternate course, and on investigating the matter more fully we found that this is indeed the case. The Grignard reagent from 1,6-dibromonaphthalene and one atom of magnesium gave α -bromonaphthalene on treatment with water and 5-bromo-2-naphthol⁷ on oxygenation. Although the reactions were not quantitative, no other products could be isolated and it appears that the Grignard reagent consists largely of the 6-MgBr derivative (VI). In the hope that the relative reactivities



might be different in a reaction of a different type, the dibromide V was heated with one mole of cuprous cyanide in pyridine solution, but the only product isolated from the resulting mixture was 1,6-dicyanonaphthalene.⁸ Although the dibromide therefore appears unsuitable for the synthesis of cholanthrene derivatives, we converted it through the ketone VII to a bromo hydrocarbon of the probable formula VIII.

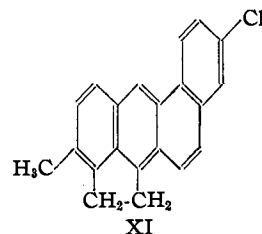
- (5) Butenandt and Schramm, *Ber.*, **68**, 2083 (1935).
 (6) Salkind, *ibid.*, **67**, 1031 (1934).
 (7) v. Braun, Hahn and Seemann, *ibid.*, **55**, 1699 (1922).
 (8) Bradbrook and Linstead, *J. Chem. Soc.*, 1739 (1936).

In order to ensure preferential reaction of a 1,6-dihalide at the 1-position rather than at position 6 it seemed necessary to employ the hitherto unknown 1-bromo-6-chloronaphthalene, and the following successful if tedious method was developed for its preparation. β -Nitronaphthalene, prepared in 10% yield from β -naphthylamine,⁹ gave on bromination according to v. Braun, Hahn and Seemann,⁷ the known 5-bromo-2-nitronaphthalene^{7,10} (IX) along with a small amount of an isomer, which probably is the 8-bromo compound.



Reduction of IX to the amine and application of the Sandmeyer reaction gave the desired 1-bromo-6-chloronaphthalene (X). Since the new compound differs in melting point from a substance (m. p. 68–69°) known to be either 1-bromo-7-chloro- or 1-bromo-6-chloronaphthalene,¹¹ the former structure can now be assigned to the substance in question.

Following the same steps as in the synthesis of the 3-methoxy compound (IV), 1-bromo-6-chloronaphthalene was converted in satisfactory yield into 3-chloro-20-methylcholanthrene (XI), and



from this the corresponding nitrile was prepared by the Rosenmund-von Braun reaction.

We are indebted to Dr. E. B. Hershberg for much helpful advice and encouragement during a period when the senior author was on leave of absence.

Experimental Part¹²

6-Methoxy-1-iodonaphthalene.—In preparing 1-acetyl-amino-6-methoxynaphthalene by the method of Butenandt and Schramm⁵ it was found convenient to conduct the

- (9) Sandmeyer, *Ber.*, **20**, 1494 (1887); Meisenheimer and Witte, *ibid.*, **36**, 4153 (1903); see also Hantzsch and Blagden, *ibid.*, **33**, 2544 (1900).
 (10) Vesely and Jakes, *Bull. soc. chim.*, [4] **33**, 952 (1923).
 (11) Guareschi, *ibid.*, [3] **1**, 647 (1889).
 (12) All melting points are corrected. Analyses by Mrs. G. M. Wellwood and Mrs. Verna R. Keevil.

acetylation in aqueous solution.¹³ The crude, moist product from the fusion of four 120-g. lots of Cleve's acid (72%) was dissolved in 1 liter of water and 87 cc. of concentrated hydrochloric acid by boiling, the solution was clarified three times with Norite until straw yellow, and treated, while efficiently stirred at 50°, with 120 cc. of acetic anhydride, followed by 100 g. of crystalline sodium acetate in 400 cc. of water. The precipitated material, collected after good cooling, weighed 52 g. (17%), m. p. 213–215°. The procedures in the literature were followed for the conversion to the methoxynaphthylamine hydrochloride⁵ and the methoxyiodonaphthalene.^{5,14}

4-Methyl-7-(6'-methoxy-1'-naphthoyl)-hydrindene (III).—The Grignard reagent prepared from 15 g. of 6-methoxy-1-iodonaphthalene and 1.5 g. of magnesium, with some benzene added to keep the product in solution, was treated while stirring with a solution of 8.5 g. of 4-methyl-7-cyanohydrindene²⁴ in ether-benzene. After refluxing for three hours water was added by drops, the ether was allowed to boil off, and 15 cc. of concentrated hydrochloric acid was added. The mixture was heated with stirring on the steam-bath until the benzene had been removed, refluxed for one and one-half hours, cooled and extracted with ether. The ether was evaporated and the product distilled. After a forerun containing some unchanged nitrile, the main ketone fraction boiled at 260–265° (3 mm.); yield 10.5 g. (63%). Crystallization from ether gave colorless prisms which softened at 82° and melted at 87.5–89°.

Anal. Calcd. for C₂₂H₂₀O₂: C, 83.51; H, 6.37. Found: C, 83.92; H, 6.16.

3-Methoxy-20-methylcholanthrene (IV).—The best results were obtained by heating the ketone III (1.43 g.), mixed with a small amount of zinc dust, in a bath maintained at 400–405° for fifteen minutes. (Without zinc dust, the yield was 6% lower.) The crude product was then distilled rapidly from the zinc and tarry residue, using an oil pump, and a solution of the material in benzene was clarified by passage through a tower of alumina. After concentration, the filtrate deposited in all 0.51 g. (38%) of satisfactory, crystalline product. The thoroughly purified substance exists in two modifications, which are characterized by the difference in crystalline forms and, less distinctly, by the melting points. A concentrated solution of the substance in benzene deposited pale yellow needles which, when collected without delay, were found to soften at 161° and melt at 166–167.5°. The dried needles do not seem to undergo change on storage, but when left in contact with the benzene mother liquor they are slowly transformed into large, thin, transparent, pale yellow plates. The plates become opaque and brighter yellow on drying, and they then melt largely at 161° but give a completely clear liquid only at 167°. The picrate crystallizes from benzene in purplish black needles, m. p. 182.5°.

Anal. Calcd. for C₂₂H₁₈O: C, 88.56; H, 6.08. Found: C, 88.47; H, 6.49. Picrate, calcd. for C₂₂H₁₈O·C₆H₄O₇N₃: N, 7.97. Found: N, 7.76.

3-Hydroxy-20-methylcholanthrene.—Constant boiling hydrobromic acid was added to a hot solution of 0.4 g. of the ether IV in 27 cc. of glacial acetic acid until the material began to precipitate at the boiling point, and the solution was refluxed for two hours, diluted with water, and extracted with benzene. After washing with bicarbonate solution and water, the benzene solution was extracted twice with dilute alkali, and the extract, with suspended sodium salt of the product, was acidified and extracted with benzene. The solution was washed and concentrated, clarified with Norite and further concentrated, and on cooling there separated 0.33 g. (87%) of needles, m. p. 220–222°. The recrystallized substance formed long, slender yellow needles, m. p. 220.5–222°. The compound is only sparingly soluble in benzene, more so in acetone, and it crystallizes from benzene-acetone in small diamond-shaped prisms, m. p. 218–220°. It is only very sparingly soluble in hot, dilute alkali; there is no coloration with alcoholic ferric chloride solution, and the solution in concentrated sulfuric acid is orange. The picrate crystallizes from benzene as deep brown needles, m. p. 201–201.5°, dec.

Anal. Calcd. for C₂₁H₁₆O: C, 88.70; H, 5.67. Found: C, 88.43; H, 5.96. Picrate, calcd. for C₂₁H₁₆O·C₆H₄O₇N₃: N, 8.19. Found: N, 8.56.

1,6-Dibromonaphthalene.—Claus and Philipson¹⁵ prepared this dibromide by converting acetyl-β-naphthylamine into the 1,6-dibromo compound,¹⁶ hydrolyzing this to the free amine,¹⁶ and eliminating the amino group through the diazo reaction.¹⁷ Since very few preparative details have been recorded in the literature it will be well to describe the procedure adopted in the present work after trying several modifications in each step.

β-Naphthylamine (36 g.) was dissolved with 21 cc. of concentrated hydrochloric acid and a few crystals of stannous chloride in 600 cc. of water by boiling, the solution was clarified, filtered, made up to a volume of 1 liter, and, while stirred mechanically at 50°, treated with 29.1 cc. of acetic anhydride and then with 37.5 g. of crystalline sodium acetate in 125 cc. of water. The colorless acetyl-β-naphthylamine, collected after cooling, weighed 42–45 g. (90–97%), m. p. 131–132.5°.

A suspension of 37 g. of acetyl-β-naphthylamine in 250 cc. of dry chloroform was stirred mechanically in a glass apparatus provided with an efficient condenser (calcium chloride-tube and trap) and a dropping funnel extending below the surface of the liquid. While cooling and stirring, 33 g. of bromine was added slowly; during this period crystals of 1-bromo-2-acetylaminonaphthalene separated but later redissolved. After about one hour any color of remaining bromine was discharged by gentle warming, and 34 g. of bromine was added slowly with stirring and while maintaining the mixture at a state of gentle reflux. The separation of the product as a granular orange precipitate causes some trouble from bumping at this stage, and the bromine color was completely discharged only after about twenty-four hours. The collected 1,6-dibromo-2-acetylaminonaphthalene after one crystallization from 2 liters

(15) Claus and Philipson, *J. prakt. Chem.*, [2] **48**, 47 (1891).

(16) See also Lawson, *Ber.*, **18**, 2422 (1885).

(13) Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, 1935, pp. 164–165, 279–280.

(14) Cohen, Cook, Hewett and Girard, *J. Chem. Soc.*, 653 (1934).

(17) See also Armstrong and Rossiter, *Proc. Chem. Soc.*, 182 (1891).

of alcohol formed colorless needles, m. p. 214.5–216°; yield 17.3–20 g. (25–29%). A suspension of 17 g. of the acetyl compound in 300 cc. of alcohol and 30 cc. of concentrated hydrochloric acid was refluxed for three hours, the material dissolving in about one-half hour and then separating as 1,6-dibromo-2-naphthylamine hydrochloride. This was collected after cooling and recrystallized from dilute alcohol; yield 15.5 g. (97%), m. p. 120–121°.

The most satisfactory of several methods of diazotization tried was that of de Milt and Van Zandt.¹⁸ Sodium nitrite (7.5 g.) was added with stirring to a cold mixture of 75 cc. of concentrated sulfuric acid and 35 cc. of water and the mixture was heated slowly and cautiously until a clear solution resulted, and this was then cooled. A solution of 14.4 g. of 1,6-dibromo-2-naphthylamine in 40 cc. of pyridine was then added in about one hour by drops with stirring to the cold solution of nitrosyl sulfuric acid (from which sodium bisulfate crystallizes), using 10 cc. of pyridine for rinsing. After stirring and cooling for two hours longer, an equal volume of alcohol was added, the solution was warmed slowly (one-half hour) and then submitted to steam distillation. The distillate was heated on the steam-bath to remove some of the alcohol and the 1,6-dibromonaphthalene was extracted with ether and distilled; b. p. 175° at 15 mm., yield 8.2 g. (60%). The substance crystallizes from alcohol in yellowish needles, m. p. 56–57° (Claus and Philipson,¹⁸ 61°; Armstrong and Rossiter,¹⁷ 57°).

Anal. Calcd. for $C_{10}H_6Br_2$: C, 41.99; H, 2.11; Br, 55.89. Found: C, 41.54; H, 2.50; Br, 55.96.

Reactivity of 1,6-Dibromonaphthalene.—One portion of a Grignard solution prepared from the dibromide and one atom of magnesium (using some benzene to keep the product in solution) was decomposed with water and the product was distilled, b. p. 280–300°. The distillate did not solidify, but a solid picrate was obtained. After several crystallizations this melted at 130–132° and did not depress the melting point of authentic α -bromonaphthalene picrate, m. p. 133–134°. Air was bubbled through a second portion of the Grignard solution at 0° for several hours, and after decomposition with acid the benzene-ether was extracted with alkali, and the acidic fraction on two crystallizations from dilute alcohol formed long, colorless needles, m. p. 105.5–107°. This corresponds to 5-bromo-2-naphthol, m. p. 105°,⁷ rather than to 6-bromo-1-naphthol, m. p. 129–130°.¹⁹ A third portion of the solution gave on carbonation an acid which, after several crystallizations from ethyl acetate, formed clusters of microcrystals, m. p. 267.5–268°, with sintering at 264°; from the above results this probably is 5-bromo-2-naphthoic acid.

In an attempt to prepare a mononitrile, 2.1 g. of 1,6-dibromonaphthalene was heated with 0.68 g. of cuprous cyanide and 2.5 cc. of pyridine for ten hours at 185° and for four hours at 200°, and on working up the product by the usual procedure^{2d} and conducting several crystallizations from alcohol, ethyl acetate, and from glacial acetic acid there was obtained eventually a substance of the constant melting point 211–213°.

(18) De Milt and Van Zandt, *THIS JOURNAL*, **58**, 2044 (1936).

(19) Fuson, *ibid.*, **47**, 516 (1925).

Anal. Calcd. for $C_{12}H_6N_2$: N, 15.7. Found: N, 15.3.

The substance corresponds in analysis and melting point with Bradbrook and Linstead's⁸ 1,6-dicyanonaphthalene, m. p. 211°.

4-Methyl-7-(5'-bromo-2'-naphthoyl)-hydrindene (VII).—The reaction of the Grignard reagent from 5 g. of 1,6-dibromonaphthalene and 0.5 g. of magnesium with 2.8 g. of 4-methyl-7-cyanohydrindene in ether-benzene was conducted as in the preparation of the ketone III and the product was distilled, b. p. 246° at 2 mm., yield 3.2 g. (50%). It crystallized from ether in the form of small, colorless prisms, m. p. 102.5–105°.

Anal. Calcd. for $C_{21}H_{17}OBr$: C, 69.05; H, 4.69. Found: C, 69.33; H, 4.74.

4'-Bromo-7-methyl-8,9-dimethylene-1,2-benzanthracene (VIII).—The ketone VII (1.1 g.) was submitted to pyrolysis in a bath at 370 \pm 5° for just eight minutes; in addition to the water produced, some hydrogen bromide was given off. The product was distilled from most of the resinous material, using a water pump, and a benzene solution of the distillate was passed through a tower of alumina, which subsequently had to be washed well with solvent to remove adsorbed material. The total yield of crystalline product melting at 241–245° was 0.4 g., but this material probably was not entirely homogeneous. After eight crystallizations from benzene or toluene the substance was obtained in an apparently pure condition, forming thin, pale yellow plates, m. p. 246.5–248°. No picrate could be obtained from benzene, toluene, or alcohol.

Anal. Calcd. for $C_{21}H_{13}Br$: C, 72.63; H, 4.35; Br, 23.02. Found: C, 73.00; H, 4.34; Br, 23.07.

1-Bromo-6-chloronaphthalene.—On brominating β -nitronaphthalene⁹ as described in the literature^{7,10} but using a small amount of chloroform as solvent, we obtained in addition to the known 5-bromo-2-nitronaphthalene, m. p. 128–130° (lit., 131°), what appeared to be an isomeric **bromo-2-nitronaphthalene**, m. p. 98–102° (calcd.: N, 5.56. Found: N, 5.73). 5-Bromo-2-naphthylamine hydrochloride⁷ was prepared by adding slowly a solution of 25 g. of stannous chloride crystals in 20 cc. of concentrated hydrochloric acid and 75 cc. of water to a stirred mixture of 7.5 g. of the nitro compound, 20 cc. of concentrated acid and 150 cc. of 50% alcohol. With gentle heating the solid soon dissolved, and on cooling 7 g. of colorless crystals separated. Recrystallization from 1 liter of water containing 15 cc. of concentrated acid gave 6.2 g. (80%) of satisfactory, tin-free salt.

For diazotization, a solution of 3.49 g. of the hydrochloride in 65 cc. of water and 6.5 cc. of concentrated hydrochloric acid was cooled to 0° with stirring and treated with 2 g. of sodium nitrite in water. After one hour at 0° 1 g. of urea (in water) was added, and after forty-five minutes the solution was stirred into a solution of cuprous chloride (from 5.25 g. of copper sulfate crystals by reduction with bisulfite) in 35 cc. of concentrated hydrochloric acid. The mixture was allowed to come to room temperature, heated on the steam-bath, cooled and extracted with ether. Distillation gave 1.62 g. (51%) of **1-bromo-6-chloronaphthalene**, b. p. 175–185° at 22 mm. On crystallization from ether the substance formed silky, colorless

needles, m. p. 41–41.5°. No picrate could be obtained in methanol or benzene solution.

Anal. Calcd. for $C_{10}H_8BrCl$: C, 49.70; H, 2.50. Found: C, 50.03; H, 2.60.

4-Methyl-7-(6'-chloro-1'-naphthoyl)-hydrindene.—The Grignard reagent from 3 g. of 1-bromo-6-chloronaphthalene and 0.32 g. of magnesium, prepared by starting the reaction with a few drops of *n*-butylmagnesium bromide solution and then refluxing overnight under nitrogen, was treated with a solution of 2 g. of 4-methyl-7-cyanohydrindene and refluxed for five hours. The product was worked up as described above and distilled, the desired ketone constituting the chief fraction, b. p. 300° at 20 mm.; yield 2.5 g. (63%). The substance formed small, colorless plates, m. p. 92–94°, from methanol.

Anal. Calcd. for $C_{21}H_{17}OCl$: C, 78.62; H, 5.34. Found: C, 78.97; H, 5.14.

3-Chloro-20-methylcholanthrene (XI).—Pyrolyzed in a bath at 400° for fifteen minutes, 2.25 g. of the above ketone gave, after rough distillation, purification in benzene solution by chromatographic adsorption and crystallization from the filtrate, 0.7 g. (33%) of the chlorohydrocarbon, m. p. 194–196.5°. Recrystallized from benzene, the compound formed yellow needles melting at 197–198.8°. No picrate was obtained in benzene or alcohol, but a rather easily dissociated di-trinitrobenzene compound crystallized from benzene-ligroin in the form of brilliant scarlet-red prisms, m. p. 165.5–166.5°.

Anal. Calcd. for $C_{21}H_{16}Cl$: C, 83.29; H, 4.99. Found: C, 83.26; H, 5.40. Di-trinitrobenzene compound, calcd. for $C_{21}H_{16}Cl \cdot 2C_6H_3O_6N_3$: N, 11.52. Found: N, 11.21.

3-Cyano-20-methylcholanthrene.—A mixture of 0.45 g. of the chloro compound XI, 0.15 g. of cuprous cyanide, and 5 cc. of pyridine in a sealed tube was warmed on the steam-bath until liquid and the tube was shaken well and heated for twenty-four hours at 200–220°, with one re-

moval for further shaking. The cooled mixture was extracted with benzene and the solution was washed with ammonia solution, water and dilute acid, filtered from a brown precipitate, washed with concentrated salt solution and concentrated. There was obtained 0.36 g. (84%) of crystalline product, m. p. 211–217°. After several recrystallizations from benzene the substance formed small yellow needles, m. p. 243–251°.

Anal. Calcd. for $C_{22}H_{15}N$: C, 90.07; H, 5.15; N, 4.77. Found: C, 89.56; H, 5.56; N, 4.52.

Summary

The general method developed in this Laboratory for the synthesis of cholanthrene and certain of its alkyl derivatives has been found satisfactory for the synthesis of the 3-methoxy and 3-chloro derivatives of methylcholanthrene. The functional substituents withstand the drastic conditions of the pyrolysis in the final step, and the chief limitation in the application of the method is that the 6-substituted 1-bromonaphthalenes required as starting materials are rather difficultly accessible. 1-Bromo-6-chloronaphthalene, required for one of the syntheses of the present work, was prepared for the first time from β -nitronaphthalene. 1,6-Dibromonaphthalene was found unsuitable for use in the synthesis of cholanthrenes because, in the reaction with magnesium, it is attacked first in the 6(β)-position rather than at the 1(α)-bromo atom.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS

RECEIVED OCTOBER 4, 1937

[CONTRIBUTION NO. 342 FROM THE FOOD RESEARCH DIVISION, U. S. CITRUS PRODUCTS STATION, U. S. DEPARTMENT OF AGRICULTURE, BUREAU OF CHEMISTRY AND SOILS]

Characteristics and Composition of Papaya Seed Oil

BY HARRY W. VON LÖESECKE AND ARTHUR J. NOLTE

The papaya (*Carica papaya*) is a melon-like fruit found growing in most tropical countries. Under ordinary conditions, the average yield of fruit per tree from commercial plantings is about 22.7 to 45.4 kg. (50 to 100 pounds). The fruit varies greatly in shape and size and may be from 10 cm. (4 inches) up to 51 cm. (20 inches) in diameter and weighing as much as 4.5 kg. (10 pounds), with an average weight of about 2 kg. (4.5 pounds). The skin is smooth, and when ripe is orange in color. The flesh varies from a light yellow to a deep salmon pink, and possesses a distinctive odor and flavor suggestive of butyric acid.

Each fruit contains about 1500 round, black, wrinkled seeds each enclosed in a gelatinous membrane. The individual seeds weigh about 0.09 g., contain 85% moisture and constitute approximately 7% of the weight of the fruit. The seeds have a distinct cress-like taste and are said to be anthelmintic, emmenagogic and carminative. They are also said to be eaten as a delicacy and as a quencher of thirst.¹

No published data could be found relative to the composition of the fatty oil in the seeds with the exception of a paper by Peckholt² who deter-

(1) Scott, "The Papaya," *Fla. State Dept. Agri. Bull.* **32** (1931).
(2) Peckholt, *Ber. Pharm. Ges.*, **13**, 366 (1903).