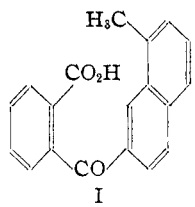
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Synthetic Routes to *meso* Substituted 1,2-Benzanthracene Derivatives[1]

BY LOUIS F. FIESER AND ARNOLD M. SELIGMAN[2]

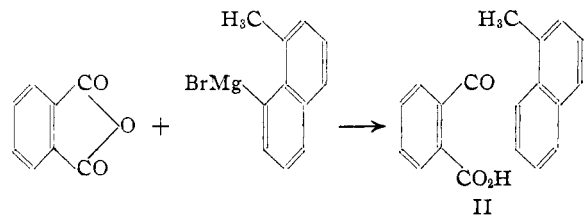
In a previous paper[3] we described the synthesis of 1′-methyl-1,2-benzanthracene[4] and 1′,10-dimethyl-1,2-benzanthracene through the intermediate keto acid (I) resulting from the condensation of phthalic anhydride with the Grignard reagent from 1-methyl-7-bromonaphthalene. We were



I

unable, however, to convert the same intermediate into the unknown 1′,9-dimethyl-1,2-benzanthracene by application of the otherwise quite general procedure of Fieser and Hershberg[5] for the synthesis of *meso*-alkyl-1,2-benzanthracenes through the benzanthranyl acetates, difficulty being experienced in the attempt to ketonize the free 1,2-benz-9-anthranol. It is not yet known if this difficulty is associated with the presence of the neighboring 1′-methyl group, for the isomerization of simpler 1,2-benz-9-anthranols has not been investigated.

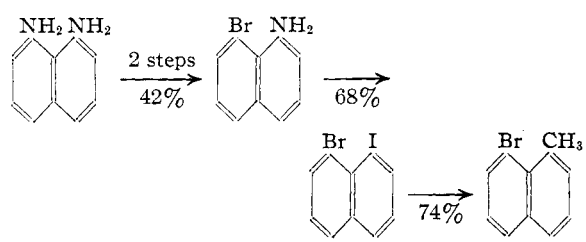
In another attempt to obtain the desired 1′,9-dimethyl compound, we undertook in the present work to try the synthetic method of Fieser and Newman,[6] for this has been employed with success in a number of instances for the introduction of alkyl groups in both *meso* positions of the 1,2-benzanthracene molecule. The preparation of the required keto acid II, an isomer of the β-naphthoyl derivative I, was accomplished without difficulty from the components indicated, but all attempts to effect the simple addition of methyl Grignard reagent to the carbonyl group of the free acid or the ester met with failure. The reac-



II

tion products were invariably unsaponifiable oils, and since the parent *o*-(1-naphthoyl)-benzoic acid is known[7] to add one mole of reagent smoothly to the carbonyl group, it seems evident that in the acid II the methyl substituent in the peri position to this group interferes with the reaction.

Before describing a third attempted synthesis, mention may be made of the methods developed for the preparation of naphthalene intermediates required for the experiments just reported and for those discussed below. 1-Methyl-8-bromonaphthalene has been obtained previously by Veselý and co-workers,[8] but by a method which does not appear to be practical for preparative purposes. A suitable method has now been found in the conversion of 1,8-diaminonaphthalene through the azimide[9] to the bromo-amine and bromo-iodo compound from which, by the action of dimethyl



sulfate on the monomagnesium derivative, the desired bromo-methyl compound was obtained in good yield. The known 1,8-dibromonaphthalene[10] can also be obtained satisfactorily from the bromo-amine. For the preparation of the hitherto undescribed 1-methyl-8-chloronaphthalene in quantity, a suitable method was developed which utilizes as starting material the 1,8-chloronitro compound, prepared easily as described by Ull-

(1) This investigation was supported in part from grants from the National Cancer Institute and the Milton Fund of Harvard University.

(2) George Cheyne Shattuck Memorial Fellow and Jeffries Wyman Scholar of the Harvard Medical School.

(3) Fieser and Seligman, THIS JOURNAL, **60**, 170 (1938).

(4) Our acknowledgment of priority[3] (Note 9) must be withdrawn, for the synthesis in London of which we had been informed was subsequently reported by Cook and Robinson, *J. Chem. Soc.*, 505 (1938), to have given 1,2-benzanthracene and not, as at first supposed, the 1′-methyl derivative.

(5) Fieser and Hershberg, THIS JOURNAL, **59**, 1028 (1937).

(6) Fieser and Newman, *ibid.*, **58**, 2376 (1936).

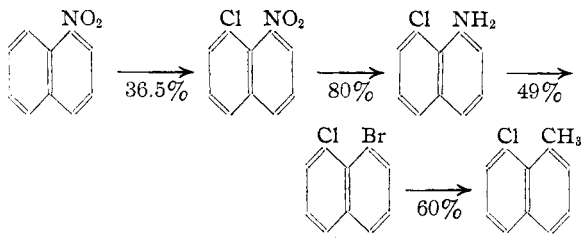
(7) Newman, *ibid.*, **59**, 1003 (1937); Cook, Robinson and Goulden, *J. Chem. Soc.*, 393 (1937).

(8) Veselý, Štursa, Olejníček and Rein, *Coll. Czechoslov. Chem. Comm.*, **2**, 145 (1930).

(9) Scholl, Seer and Weitzenböck, *Ber.*, **43**, 2202 (1910).

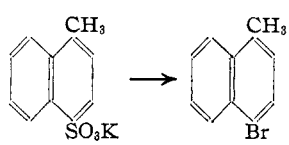
(10) Meldola and Streatfeild, *J. Chem. Soc.*, **63**, 1054 (1893).

mann and Consonno[11] and by Adams and Steele.[12]

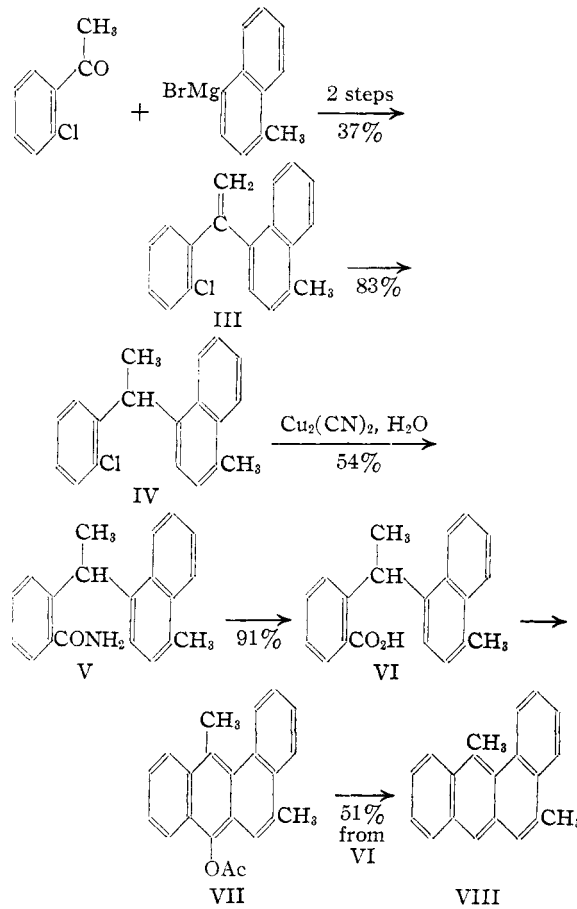


This was reduced with iron powder[12] and the amine converted into 1-chloro-8-bromonaphthalene, which E. Bergmann and Hirshberg[13] obtained in low yield by another method. Methylation of the monomagnesium derivative then gave the desired 1-methyl-8-chloronaphthalene.

For 1-methyl-4-bromonaphthalene, also required as an intermediate, the best previous method of preparation has been by direct bromination,[14] which affords only moderately pure material in 55% yield. We have found that material of excellent quality can be prepared easily by the action of bromine in aqueous solution on potassium 1-methylnaphthalene-4-sulfonic acid.



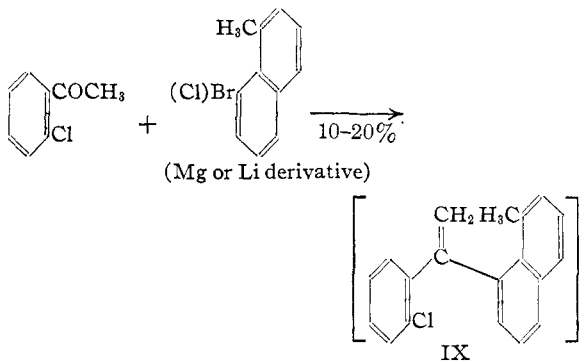
With the failure of the above attempts to apply two otherwise general methods for the synthesis of *meso*-alkyl-1,2-benzanthracenes, attention was turned to a new scheme of synthesis. In order to test the method in a case free from possible complications associated with the presence of a *peri*-methyl group and requiring readily accessible intermediates, we undertook the synthesis of the hitherto unknown 3,9-dimethyl-1,2-benzanthracene. As shown in the chart, 1-methyl-4-naphthylmagnesium bromide was condensed with *o*-chloroacetophenone and the crude carbinol dehydrated. The unsaturated intermediate III slowly absorbed the required amount of gas on hydrogenation in glacial acetic acid solution, and the saturated product (IV) when heated with cuprous cyanide and water in pyridine solution afforded the amide V. This was converted by isoamyl nitrite in acetic acid solution at 40° into the acid VI, and acetylative cyclization[5] to VII and reduction gave the desired 3,9-dimethyl-1,2-benzanthracene.



On the strength of the success of this one application of the synthetic method, various other applications and modifications are being investigated. It should be possible to transpose the carbonyl group from the benzene to the naphthalene nucleus in exchange for the magnesio-halide group, and by utilizing both α- and β-substituted naphthalene derivatives provision would be made for the introduction of alkyl groups in either of the two *meso* positions.

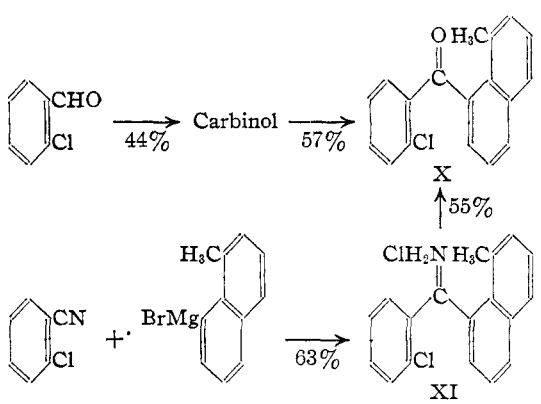
In the particular application for which the synthesis was designed, difficulties were encountered and the final goal of obtaining the 1′,9-dimethyl compound has not yet been attained. Tried under various conditions, the condensation of *o*-chloroacetophenone with the Grignard reagent from 1-methyl-8-bromonaphthalene proceeded poorly. After dehydration there was obtained an oil which appeared to consist largely of the expected compound (IX), but the yield was at best only 20%. With the lithium derivative, pre-

(11) Ullmann and Consonno, *Ber.*, **35**, 2802 (1902).
(12) Adams and Steele, THIS JOURNAL, **52**, 4528 (1930).
(13) E. Bergmann and Hirshberg, *J. Chem. Soc.*, 331 (1936).
(14) F. Mayer and Sieglitz, *Ber.*, **55**, 1835 (1922); R. Robinson and H. W. Thompson, *J. Chem. Soc.*, 2015 (1932).



pared from 1-methyl-8-chloronaphthalene, the yield was still lower (10%). Hydrogenation of IX proceeded extremely slowly, and attempts to convert the saturated product into a nitrile, amide, or acid with cuprous cyanide and anhydrous or aqueous pyridine were fruitless.

In the hope of getting a better yield of perhaps purer material, we next condensed *o*-chlorobenzaldehyde with 1-methyl-8-naphthylmagnesium bromide and oxidized the resulting carbinol to the ketone X. The yield in the Grignard reaction



was better than with *o*-chloroacetophenone but still low, and in order to obtain a product of unquestioned purity we investigated the alternate synthesis from *o*-chlorobenzonitrile. The Grignard reaction in this case proceeded quite well, but a difficulty was encountered in that the crystalline ketimine hydrochloride XI proved to be extremely resistant to hydrolysis. This is a clear indication of the hindering action of the *peri*-methyl group and the *ortho*-chloro substituent. After less drastic methods had failed, hydrolysis was accomplished by heating the ketimine hydrochloride with a formic–sulfuric acid mixture in a pressure tube at 150°, and this afforded a crystalline ketone (X) of the expected composition. It was hoped that in the next step a methyl group could be introduced by interaction of the ketone with methylmagnesium chloride. A reaction indeed occurred, but the oil obtained after dehydration with potassium bisulfate boiled over a 20° range and contained a much higher proportion of carbon and hydrogen than expected. The material took up hydrogen in the presence of Adams catalyst without formation of hydrogen chloride, but the product was a mixture which gave no crystalline picrate and which contained less than one-fourth the amount of chlorine for the expected isomer of VI. Halogen is therefore eliminated in the Grignard reaction or in the dehydration. The difficulty must be associated with the highly hindered character of the carbonyl group of the ketone; it seems possible that the chlorine atom is displaced either by direct coupling or as the result of a forced addition of the Grignard reagent involving a conjugated nuclear position. In any case it is evident that this modification of the synthetic method is not applicable to the case at hand.

We are indebted to Frederick C. Novello for valuable assistance in some of the preparative work.

Experimental Part[15]

1. Preparation of Naphthalene Derivatives

8-Bromo-1-naphthylamine.—*Forty-five grams of 1,8-diaminonaphthalene was dissolved by heating in 3 liters of water containing 105 cc. of concentrated hydrochloric acid and the solution was filtered and cooled to 0–5°. While stirring the solution at this temperature, 20.1 g. of sodium nitrite in 500 cc. of water was added over a period of forty-five minutes. After stirring for fifteen minutes longer the mixture was allowed to stand overnight in the cold room to facilitate the filtration of the brown-red azimino compound which separated. The precipitate was collected, dried at 25–45°, and used without further purification. The combined material from three 45-g. lots of diamine was stirred mechanically in a large beaker with 900 cc. of constant boiling hydrobromic acid and, while heating on the hot-plate, 36 g. of fiery red, heat-treated copper bronze was added. The mixture was brought to the boiling point and held there until nitrogen was no longer evolved and a floating sludge had separated. The mixture was then diluted with 2 liters of water, heated to boiling, and filtered, and the residue was extracted twice with boiling water. The total aqueous extract was cooled, neutralized with ammonia solution, and extracted with ether. The ethereal solution was washed, separated from the bulk of the aqueous layer, filtered by suction to remove suspended solid, washed, dried, and evaporated. The residue distilled largely at 155° at 4 mm., yielding 80 g. (42%) of nearly colorless, crystalline 8-bromo-1-naphthyl-*

(15) All melting points are corrected. Analyses by Lyon Southworth and the Arlington Laboratories.

amine. A sample purified by crystallization from petroleum ether, but not distilled, melted at 87–88°. Meldola and Streatfeild[10] prepared the compound from the mixture obtained by the nitration of α-naphthylamine and reported the m. p. 89–90°.

When dull polished copper powder was used the yield was much lower (20%) and considerable α-naphthylamine was produced; electrolytic copper gave a particularly poor result, and it appears that the coating of copper oxide produced in the heat treatment is important for catalysis of the desired reaction.

1-Bromo-8-iodonaphthalene.—A solution of 80 g. of the distilled bromo-amine in 30 cc. of concentrated sulfuric acid and 1 liter of water was cooled to 0° and diazotized, while stirring, with 26 g. of sodium nitrite in 50 cc. of water. After standing for one-half hour, the solution was added to a stirred solution of 90 g. of potassium iodide in 75 cc. of water and the stirred solution was slowly heated until a dark oil separated. This solidified on cooling; the aqueous liquor was bleached with sodium bisulfite and decanted. The residue was dried and distilled (trap of solid potassium hydroxide), leaving a tarry residue and giving 95 g. of solid distillate. Crystallization from alcohol gave 81.5 g. (68%) of satisfactory material in the form of heavy tan plates. A sample crystallized three times from alcohol gave pale tan plates, m. p. 99–100°.

Anal. Calcd. for $C_{10}H_6BrI$: C, 36.06; H, 1.82. Found: C, 36.21; H, 1.86.

1-Methyl-8-bromonaphthalene.—The Grignard reagent from 65 g. of 1-bromo-8-iodonaphthalene was prepared by adding the solid in a single portion to a stirred suspension of 5 g. of magnesium in 200 cc. of ether, after thorough cooling by stirring in an ice-bath. The mixture was allowed to warm until a vigorous reaction was under way and then the temperature was controlled by cooling in such a way as to allow the magnesium to dissolve completely in thirty to forty-five minutes. (When the reaction was allowed to proceed more rapidly the product obtained after methylation contained considerable 1,8-dimethylnaphthalene and unchanged bromo-iodo compound.) The solution was cooled and stirred and treated with 60 g. of freshly distilled dimethyl sulfate in 200 cc. of benzene, which at once precipitated a yellow complex. After removing some of the ether by distillation, the mixture was refluxed overnight (a shorter period resulted in a poor yield). Dilute hydrochloric acid was then added and the benzene layer was washed and heated with 200 cc. of 10% sodium hydroxide. The organic solvent was allowed to distil and the oil was extracted with ether. Distillation gave 35 g. of solid product boiling at 132° (4 mm.), and when crystallized from alcohol this formed colorless plates, m. p. 76–78°; yield, 32 g. (74%). A recrystallized sample melted at 77–78°; Veselý and co-workers[8] report the m. p. 80°.

1,8-Dibromonaphthalene was obtained by treating 15 g. of 8-bromo-1-naphthylamine, diazotized in hydrobromic acid solution, with cuprous bromide and hydrobromic acid; yield, 11 g. (57%). It formed colorless plates from alcohol, m. p. 109–110°; Meldola and Streatfeild[10] give 108.5–109°.

It was noted that the dibromide reacts very slowly with magnesium and gives a very sparingly soluble, crystalline Grignard derivative.

1 - Chloro - 8 - bromonaphthalene.—α - Nitronaphthalene (550 g.) was chlorinated as described in the literature[11,12] in the presence of ferric chloride (12 g.) at 40–60° until the gain in weight was 130 g. and, after cooling, the crystalline **1-chloro-8-nitronaphthalene** was collected on a suction filter, pressed well, and crystallized from alcohol; yield, 240 g. (36.5%), m. p. 89–91°. This material (240 g.), reduced according to Adams and Steele,[12] gave 165 g. (80%) of **8-chloro-1-naphthylamine,** m. p. 90°.

The diazotization of 165 g. of the amine in 1.5 liters of water and 250 cc. of constant boiling hydrobromic acid was accomplished with 70 g. of sodium nitrite. The solution was added to 300 g. of cuprous bromide in 250 cc. of constant boiling hydrobromic acid, 50 cc. of water, 40 g. of sodium bromide, and 35 g. of copper reduced by hydrogen. After heating on the steam-bath to decompose the complex the dark oil separating was washed in ethereal solution with acid and alkali, dried and distilled in vacuum. After a fore-run containing 20 g. of α-chloronaphthalene, the chlorobromonaphthalene distilled at 154° (4 mm.) and solidified on cooling; yield, 110 g. (49%). After two crystallizations from alcohol the substance formed heavy, colorless leaves, m. p. 96.5–97° (compare Bergmann and Hirshberg: 94–95°). The **picrate** formed stout yellow needles from alcohol, m. p. 130.5–131.5°.

1-Methyl-8-chloronaphthalene.—The Grignard reagent was prepared from 49 g. of the above chlorobromo compound in ether and 5.2 g. of magnesium, the mixture being stirred and refluxed for twenty-four hours with the addition of benzene, as required, to keep the Grignard compound from crystallizing too extensively. A benzene solution of 60 g. of freshly distilled dimethyl sulfate was added, the ether was largely removed, and after refluxing for twenty-four hours the product was worked up as described for the methylbromo compound. It distilled at 125° (4 mm.); yield, 21.5 g. (60%). The substance crystallizes from alcohol in colorless leaflets, m. p. 68–69°. The **picrate** forms fine, orange-yellow needles, m. p. 138.5–139.5°.

Anal. Calcd. for $C_{11}H_9Cl$: C, 74.79; H, 5.13. Found: C, 75.03, 75.14; H, 5.34, 5.44.

1-Methyl-4-bromonaphthalene.—A solution of 210 g. of α-methylnaphthalene in 375 cc. of concentrated sulfuric acid was allowed to stand at room temperature for five hours and diluted with an equal volume of water. The sulfonic acid which separated on cooling was collected and dissolved in 1 liter of hot water; 225 g. of potassium chloride was dissolved in the solution, and the potassium salt which crystallized on cooling was collected and brominated in two portions, without being dried. Each portion was dissolved in 1.4 liters of water and treated with stirring at 50° with a solution of 70 g. of bromine and 100 g. of sodium bromide in 300 cc. of water. A considerable amount of the bromo compound separated at once as an emulsion and soon settled as an oil. The aqueous solution was decanted and treated with a fresh portion of 20 g. of bromine and 30 g. of sodium bromide in 100 cc. of water. The solution was at once neutralized with sodium bisulfite and the oil allowed to collect. The aqueous solution was extracted once with ether, and the ethereal solution of the oil was washed with sodium bisulfite solution, acid and alkali, dried and evaporated. The product distilled at

146° (8 mm.); total yield from 210 g. of hydrocarbon, 92 g. (28%). The redistilled material melted at 7°; picrate, m. p. 128–129°. Robinson and Thompson[14] give the m. p. 5.5–6°; picrate, m. p. 126–127°.

2. Second Attempted Synthesis

o - (8 - Methyl - 1 - naphthoyl) - benzoic Acid (II).—The formation of the Grignard reagent from 22 g. of 1-methyl-8-bromonaphthalene and 2.6 g. of magnesium proceeded slowly, apparently because of the separation of colorless crystals of the reagent, and it was necessary to reflux and stir the mixture for two days to complete the reaction. The suspension was added during one-half hour to a refluxing benzene (200 cc.) solution of 25 g. of phthalic anhydride, giving a yellow complex. Refluxing was continued for two and one-half hours, allowing the ether to evaporate. On decomposition with dilute hydrochloric acid the keto acid II separated in a crystalline condition and was collected; a further small amount was extracted from the benzene with soda. The substance crystallized from acetic acid–alcohol in heavy, colorless prisms of high purity; yield, 19 g. (66%). A sample recrystallized from alcohol melted at 231.5–232.5°.

Anal. Calcd. for $C_{19}H_{14}O_3$: C, 78.62; H, 4.86. Found: C, 78.48; H, 4.78.

In a typical attempted Grignard reaction 18.5 g. of powdered keto acid was added to the reagent from 5 g. of magnesium and excess methyl chloride, benzene was added, and the mixture was refluxed for two days. There was obtained 1.5 g. of unchanged keto acid and 16.5 g. of an unsaponifiable oil. The results were the same when the refluxing was shorter, except that more keto acid was recovered. The neutral oil gave no acidic product on prolonged treatment with amalgamated zinc and hydrochloric–acetic acid. Similar results were obtained with the methyl ester of II, prepared with diazomethane, m. p. 153–154°.

3. Synthesis of 3,9-Dimethyl-1,2-benzanthracene

α - (o - Chlorophenyl) - α - (4 - methyl - 1 - naphthyl)-ethylene (III).—For the preparation of the required **o-chloroacetophenone** the carbinol obtained from 192 g. of freshly distilled *o*-chlorobenzaldehyde and methylmagnesium chloride was added in portions to a stirred solution of 270 g. of anhydrous sodium dichromate and 122 cc. of concentrated hydrochloric acid in 1350 cc. of water. The temperature rose to 55°, and after two hours the solution was diluted and extracted with ether. After washing and drying, the product distilled at 113° (14 mm.); yield, 167 g. (79%); semicarbazone, m. p. 181–182°.

The Grignard reagent was prepared from 68.5 g. of pure 1-methyl-4-bromonaphthalene and 7.8 g. of magnesium, adding benzene as required to keep the product from crystallizing. After six hours 48 g. of *o*-chloroacetophenone in 75 cc. of benzene was added slowly, the ether was displaced with benzene, and refluxing was continued for fifteen hours. (Refluxing for four hours gave a poorer yield.) After washing the product in ether–benzene solution with dilute acid and water, the solvent was removed and the material distilled. A sizable fore-run was found to contain some *o*-chloroacetophenone and considerable α-methylnaphthalene, identified as the picrate; the residue, consisting largely of the carbinol, partially lost water on attempted distillation. It was therefore heated with 7 g. of potassium bisulfate at 200° for ten minutes and then distilled in vacuum, giving 37 g. of viscous yellow oil. Redistilled, the product boiled at approximately 200° (4 mm.); yield, 31.6 g. (37%).

Anal. Calcd. for $C_{19}H_{15}Cl$: C, 81.84; H, 5.42. Found: C, 81.05; H, 5.53.

α - (o - Chlorophenyl) - α - (4 - methyl - 1 - naphthyl)-ethane (IV).—The above oil (31.6 g.) was hydrogenated smoothly if slowly in glacial acetic acid solution using Adams catalyst (0.6 g.) in twelve hours. (In previous attempts no absorption of hydrogen was observed when alcohol or ethyl acetate was used as solvent, with less pure material in acetic acid or with copper chromite catalyst at 250° in the high pressure bomb.) Distillation gave 26.7 g. (83%) of a viscous, pale yellow oil, b. p. 175° (4 mm.). A sample of the oil solidified after standing for several days and this formed small clusters of colorless needles from methanol, m. p. 66.5–67.5°. The oil was used for analysis.

Anal. Calcd. for $C_{19}H_{17}Cl$: C, 81.25; H, 6.10. Found: C, 80.99; H, 6.26.

It seems advisable to use a considerable amount of catalyst in order to complete the hydrogenation as rapidly as possible, and the reaction should be stopped after absorption of the theoretical amount of gas.

α - (o - Amidophenyl) - α - (4 - methyl - 1 - naphthyl)-ethane (V).—A mixture of 25 g. of the chloro compound IV, 15 g. of cuprous cyanide, 70 cc. of pyridine, and 8.5 cc. of water was heated in a Pyrex tube in an electric furnace at 220° for forty-eight hours. The resulting mixture, which was lighter in color than at the beginning, was washed out with benzene and ammonia solution, filtered from cuprous salts, and the benzene layer was separated, washed and concentrated. The amide crystallized from this solution in a satisfactory condition; yield, 14 g. (54%). The amount of acid obtained from the ammonia extract was negligible. Crystallized from ether, the amide formed colorless prisms, m. p. 171–172°.

Anal. Calcd. for $C_{20}H_{19}ON$: C, 83.02; H, 6.62. Found: C, 83.19; H, 6.79.

The benzene mother liquor afforded an oil (10 g.) which probably contained some of the corresponding nitrile, but on attempting to hydrolyze this the tube exploded.

α - (o - Carboxyphenyl) - α - (4 - methyl - 1 - naphthyl)-ethane (VI).—For hydrolysis the amide (13 g.) was treated in glacial acetic acid solution (80 cc.) with isoamyl nitrite (40 cc., in portions) at 40° for two days. The solution was evaporated and the residual oil taken into ether, and after washing with water the acid was extracted with soda solution. The ether layer afforded 2 g. of unchanged amide. The acid liberated on acidification of the soda extract was taken into ether and the solution was washed, dried, and evaporated, when the product crystallized; yield, 10 g. (91%, on the basis of material consumed). A sample crystallized from ether–petroleum ether formed nearly colorless prisms, m. p. 190.5–191.5°.

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 82.75, H, 6.25. Found: C, 82.15; H, 6.57.

Cyclization and Reduction to 3,9-Dimethyl-1,2-benzanthracene.—A mixture of 10 g. of the acid VI, 1 g. of zinc

chloride, 75 cc. of acetic acid, and 50 cc. of acetic anhydride was refluxed for one hour, water was added cautiously to decompose excess anhydride, and the solution was diluted and extracted with ether. No acidic material was removed on extraction with soda, and on drying and evaporating the ethereal solution there was left a residue which set to a stiff glass but which failed to crystallize. This material, which apparently consisted of the 1,2-benz-10-anthranyl acetate VII in crude form, was reduced directly by refluxing in 20 cc. of toluene with 10 g. of zinc dust (washed with an aqueous solution of 0.4 g. of copper sulfate) and 100 cc. of 10% sodium hydroxide for seven hours. The toluene was then removed by distillation and the aqueous liquor and zinc residue were extracted thoroughly with ether. This was washed with acid, dried, and evaporated, and the residual oil was dissolved in an alcoholic solution of picric acid. The picrate crystallized on cooling in dark crimson needles, m. p. 134–135°; yield, 8.6 g. (51%). For recovery of the hydrocarbon 1.9 g. of this picrate was passed in benzene solution through a tower of alumina, and the product collected from the filtrate was crystallized from methanol, giving 0.7 g. of pure 3,9-dimethyl-1,2-benzanthracene. The hydrocarbon forms pale yellow platelets, m. p. 93–93.5°; it dissolves in concentrated sulfuric acid with a crimson color. The best sample of **picrate** melted at 137–138°. The **trinitrobenzene derivative** formed crimson needles from benzene–ligroin, m. p. 145°.

Anal. Calcd. for $C_{20}H_{16}$: C, 93.70; H, 6.30. Found: C, 93.47; H, 6.49. Trinitrobenzene derivative, calcd.: N, 8.96. Found: N, 9.10.

Oxidation of the hydrocarbon (0.1 g.) with sodium dichromate (2 g.) in glacial acetic acid solution gave yellow needles of 3-methyl-1,2-benzanthraquinone, m. p. (after crystallization from methanol), 178.5–179.5° (positive vat test, green in sulfuric acid). Scholl and Tritsch[16] give the m. p. 176–177°.

4. Third Attempted Synthesis

Reaction Product IX: α-(*o*-Chlorophenyl)-α-(8-methyl-1-naphthyl)-ethylene (?).—The Grignard reagent was prepared as described above from 50 g. of 1-methyl-8-bromonaphthalene and 5.7 g. of magnesium (refluxing for thirty-six hours with the addition of 100 cc. of benzene) and treated with 45 g. of *o*-chloroacetophenone, added slowly in benzene solution. The ether was displaced with benzene, refluxing was continued for thirty hours, and after collection of the product it was dehydrated with potassium bisulfate and distilled twice, giving 13 g. (20%) of an orange oil, b. p. 200° (4 mm.). Using the lithium derivative from 1-methyl-8-chloronaphthalene the yield was 9.5%. The unsaturated compound very slowly absorbed the calculated quantity of hydrogen in acetic acid solution, but no pure reaction products could be obtained on heating the product with cuprous cyanide in pyridine, with or without the addition of water.

1-Methyl-8-(*o*-chlorobenzoyl)-naphthalene (X). (a) From *o*-Chlorobenzaldehyde.—The Grignard reagent from 27 g. of 1-methyl-8-bromonaphthalene was treated with 16 g. of freshly distilled *o*-chlorobenzaldehyde in benzene, the ether was largely displaced by benzene, and refluxing was continued for four hours. Distillation gave 15 g. (44%) of the **carbinol** as a viscous, pale yellow oil, b. p. 210° (4 mm.). The yield from the lithium compound was poorer (23%).

Anal. Calcd. for $C_{18}H_{15}OCl$: C, 76.47; H, 5.35. Found: C, 77.01; H, 5.34.

For oxidation, 21 g. of the carbinol in 30 cc. of benzene was added to a stirred solution of 40 g. of sodium dichromate, 30 cc. of glacial acetic acid, and 50 cc. of concentrated sulfuric acid in 160 cc. of water (temperature, 25–30°), and stirring was continued for six hours. The ketone obtained distilled as a viscous oil at 205° (4 mm.); yield, 12 g. (57%).

(b) From *o*-Chlorobenzonitrile.—The Grignard reagent from 66 g. of 1-methyl-8-bromonaphthalene was mixed with 26 g. of *o*-chlorobenzonitrile in benzene, and after refluxing for sixteen hours dilute hydrochloric acid was added and the crystalline ketimine hydrochloride (XI) was collected and washed with cold water, alcohol and ether; yield, 60 g. (63%). This salt, which is moderately soluble in hot water, was recovered unchanged after refluxing with hydrochloric acid at various concentrations. Hydrolysis finally was accomplished by sealing 10-g. portions in Pyrex tubes with 20 cc. of formic acid, 20 cc. of water, and 0.5 cc. of concentrated sulfuric acid and heating each tube in turn in a high-pressure steel bomb with application of a gas pressure outside the tube of 500–800 lb. (33–53 atm.) (at 25°). Heating was continued at 150° for three hours, the pressure was released from the cooled bomb, and the tube opened cautiously (gas pressure). The dark oil which had separated was extracted with ether, washed, dried, and distilled: b. p. 205° (4 mm.); yield, 29 g. (55%). The analytical sample solidified on standing.

Anal. Calcd. for $C_{18}H_{13}OCl$: C, 77.01; H, 4.66. Found: C, 76.53; H, 4.83.

As recorded in the theoretical part, the reaction of this ketone with excess methylmagnesium chloride in benzene solution (refluxing overnight) did not proceed normally. The reaction product from 29 g. of the ketone was dehydrated with 5 g. of potassium bisulfate at 200°, and after three distillations the resulting viscous oil boiled at 170–190° (16.5 g.). Analyses of this material gave: C, 86.5; H, 6.6 (calcd.: C, 81.8; H, 5.4). In acetic acid, using Adams catalyst, the material absorbed somewhat more than the expected amount of hydrogen in sixteen hours, but the product distilled at 4 mm. in the range 150–195°. A middle fraction had the composition: C, 85.2; H, 8.0; Cl, 4.1 (calcd.: C, 81.2; H, 6.1; Cl, 12.6). The oil failed to yield a solid picrate.

(16) Scholl and Tritsch, *Monatsh.*, **32**, 997 (1911).

Summary

In attempts to prepare the unknown 1′,9-dimethyl-1,2-benzanthracene, two otherwise general methods for the synthesis of *meso*-alkyl-1,2-benzanthracenes have been tried without success, the difficulty in at least one case being attributable to steric interference from the *peri*-methyl group. A new scheme for the synthesis of hydrocarbons of the type indicated has been devised and found entirely satisfactory for the prepara-

tion of 3,9-dimethyl-1,2-benzanthracene, and it offers promise of being capable of wide application and modification. Two variations of the new method, however, were applied without success to the problem at hand, steric hindrance again proving to be an obstacle in essential stages of the synthesis.

In the course of the work, practical methods were developed for preparing the 1,8-methylbromo, methylchloro, chlorobromo, bromoiodo, and dibromo derivatives of naphthalene, and 1-methyl-4-bromonaphthalene.

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Brassicasterol. I. Empirical Formula and Hydrogenation

BY ERHARD FERNHOLZ AND HOMER E. STAVELY

Brassicasterol is a phytosterol first isolated from rapeseed oil by Windaus and Welsch[1] and has since received little attention. Schmid and Waschkav[2] reported a crystallographic examination of the tetrabromide of brassicasteryl acetate and found it to be similar to the corresponding derivative of stigmasterol.

The brassicasterol reported by Windaus and Welsch[1] was isolated from a technical waste by-product of rapeseed oil refining. We thought it possible that the sterol had not originally been present in the raw oil, but had resulted from isomerization of stigmasterol in the presence of the concentrated sulfuric acid used in the refining process. In order to remove this uncertainty in the present investigation, we have used an unrefined rapeseed oil of Japanese origin.[3] However, the brassicasterol isolated by us had practically the same physical constants as those given by Windaus and Welsch.[1] Brassicasterol is, therefore, very similar to, but not identical with stigmasterol.

From analyses of the tetrabromide acetate and propionate Windaus and Welsch[1] gave an empirical formula $C_{28}H_{46}O$ for brassicasterol. Experience has shown that combustions of bromides do not give analyses sufficiently accurate to distinguish between homologs. Dinitrobenzoates[4] give more reliable data for this purpose, even though the analytical differences between homologs are smaller. Analytical results of brassicasteryl dinitrobenzoate and brassicastyl dinitrobenzoate indicate an empirical formula $C_{29}H_{48}O$ for brassicasterol, identical with that of stigmasterol.

(1) Windaus and Welsch, *Ber.*, **42**, 612 (1909).
(2) Schmid and Waschkav, *Monatsh.*, **48**, 139 (1927).
(3) Courtesy of Welch, Holme and Clark.
(4) Windaus, Von Werder and Oeshaider, *Ber.*, **65**, 1006 (1932).

Catalytic hydrogenation of brassicasterol gave a saturated sterol not identical with stigmasterol, as shown in Table I. Hence the difference between

TABLE I

Substance	M. p., °C.	$[\alpha]^{25}D$
Stigmastanol	137	+25
Stigmastyl acetate	131	+15
Stigmastyl *m*-dinitrobenzoate	215	+13
Brassicastanol	142	+24
Brassicastyl acetate	143	+15
Brassicastyl *m*-dinitrobenzoate	202	+14

stigmasterol and brassicasterol does not lie in the position of a double bond, but in the carbon skeleton.

Brassicastanol is also different from ostreastanol.[5]

Experimental

Isolation of Brassicasterol.—Unrefined rapeseed oil (6.8 kg.) was saponified with methanolic potassium hydroxide and the unsaponifiable matter extracted with ether, giving 20.4 g. of crude crystalline sterol after crystallization from ethanol. It was acetylated with acetic anhydride and brominated according to the method of Windaus and Welsch.[1] The yield of tetrabromide was much less than that reported by these authors; 1.1 g. of pure tetrabromide was obtained; m. p. 205° (dec.). The bromination mixture had to be kept for several days for complete precipitation of the tetrabromide.

Debromination yielded an acetate whose m. p. could not be raised above 152° (Windaus and Welsch[1] reported 157–159°); $[\alpha]^{22}D$ −65° (20.0 mg. in 2.06 cc. chloroform, $\alpha^{26}D$ −0.63, 1-dm. tube) (not previously reported).

By saponification brassicasterol was obtained; m. p. 146°; $[\alpha]^{22}D$ −61° (Windaus and Welsch reported m. p. 148°, $[\alpha]D$ −64°).

Brassicasteryl *m*-Dinitrobenzoate.—Brassicasterol (0.45 g.) and an excess of *m*-dinitrobenzoyl chloride in pyridine were heated on a steam-bath. The ester was recrystallized from benzene by addition of ethanol giving rhombic plates,

(5) Bergmann, *J. Biol. Chem.*, **104**, 553 (1934).