

centrated solution of stannous chloride in dilute acetic acid, added by drops until a test portion of the solution gave with water a precipitate which dissolved completely in dilute alkali. On gradual dilution with water the solution deposited colorless needles of the reduction product (0.7 g., 96%). The phenanthrol formed long needles, m. p. 130–131°, from dilute alcohol.

*Anal.** Calcd. for $C_{14}H_7OCl_4$: Cl, 35.78. Found: Cl, 35.74.

The acetate crystallized from alcohol as lustrous plates, m. p. 164–165°.

*Anal.** Calcd. for $C_{16}H_9O_2Cl_3$: Cl, 31.35. Found: Cl, 31.15.

1(?),9(or 10)-Dichloro-3,4-phenanthrenequinone (XIV).—A solution of 0.35 g. of the trichlorophenanthrol in 8 cc. of glacial acetic acid was oxidized with 3 cc. of concentrated nitric acid added all at once. The solution became red immediately and then began to darken; after three to four minutes it was gradually diluted with an equal volume of water, thus precipitating the quinone in a microcrystalline condition. Recrystallization from glacial acetic acid gave small, dark red needles melting at 239–240° dec.; yield, 0.22 g. (67%).

Anal. Calcd. for $C_{14}H_6O_2Cl_2$: C, 60.65; H, 2.18. Found: C, 60.53; H, 2.53.

1(?),3,4 - Triacetoxo - 9(or 10) - chlorophenanthrene.—A suspension of 90 mg. of the quinone XIV in 6 cc. of acetic anhydride containing 6 drops of concentrated sulfuric acid was shaken at intervals and frequently warmed on the steam-bath. The material dissolved in about six hours, and after standing overnight the red-yellow solution was treated with water. One crystallization from acetic acid gave 70 mg. of yellowish rods, and after further crystallizations from alcohol the compound was obtained as slender, colorless needles, m. p. 230–231°.

*Anal.** Calcd. for $C_{20}H_{16}O_6Cl$: Cl, 9.17. Found: Cl, 9.65.

Summary

3-Bromo-1,2-phenanthrenequinone and 2-bromo-3,4-phenanthrenequinone add dienes readily and the addition products can be converted in good yield into 3,4-benzphenanthrenequinones and chrysenes, respectively.

From a preliminary study of the chlorination of 3-phenanthrol it appears that the substance not only is attacked in the hydroxylated ring but adds chlorine at the 9,10-position.

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CAMBRIDGE, MASS.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

10-Substituted 1,2-Benzanthracene Derivatives

BY LOUIS F. FIESER AND E. B. HERSHBERG¹

The observation that 10-methyl-1,2-benzanthracene² is a potent carcinogenic agent comparable with cholanthrene and methylcholanthrene in the rapidity and regularity with which it produces tumors in experimental animals³ has made it a matter of considerable interest to investigate additional 10-substituted derivatives of the tetracyclic hydrocarbon. The 10-methyl derivative contrasts strikingly with 1,2-benzanthracene itself, for in experiments conducted at the Royal Cancer Hospital the latter hydrocarbon has produced only one tumor (papilloma) in eighty mice tested.⁴ Since compounds of more complex structure than the methyl derivative, namely, the 10-isopropyl and 10-benzyl compounds, have been tested by the English investigators⁴ with entirely negative results, it is impor-

tant to determine whether 10-methyl-1,2-benzanthracene occupies a unique position or is one of a possibly limited series of homologs possessing some carcinogenic activity. A series of closely related hydrocarbons of graduated potency would offer many interesting possibilities for biological and chemical experimentation.

None of the synthetic methods hitherto employed for the preparation of 10-alkyl-1,2-benzanthracenes seemed adequate for the purpose at hand without some modification. The synthesis of Fieser and Newman² provides a quite satisfactory, if somewhat lengthy, route to the 10-methyl compound, but it suffers from the limitation that considerable reduction occurs as a side reaction in the condensation of higher alkylmagnesium halides with 2-*o*-toluyl-1-naphthoic acid. Cook⁵ obtained the 10-benzyl compound in small yield by the action of benzyl chloride on 1,2-benzanthracene in the presence of zinc dust, but direct alkylation clearly is out of the question as a general method. A third synthesis,

(1) Lilly Research Fellow.

(2) Fieser and Newman. *THIS JOURNAL*, **58**, 2376 (1936).

(3) Fieser and Hershberg. *ibid.*, **59**, 394 (1937); L. F. Fieser, M. Fieser, Hershberg, Newman, Seligman and Shear. *Am. J. Cancer*, **29**, 260 (1937).

(4) Barry. Cook, Haslewood, Hewett, Hieger and Mayneord. *Proc. Roy. Soc. (London)*, **B117**, 318 (1935).

briefly investigated by Cook^{5,6} with only moderate success, consists in the addition of a Grignard reagent to 1,2-benz-10-anthrone (IV, below) and the dehydration of the resulting dihydroanthranol. Cook prepared 10-benzyl⁵ and 10-isopropyl-1,2-benzanthracene⁶ in unspecified yield by this method. Recently, Cook, Mrs. Robinson and Goulden^{5a} have overcome earlier difficulties⁵ and succeeded in preparing the 10-methyl compound in the same way. The 1,2-benz-10-anthrone used in these experiments was a crude product prepared⁵ by heating 2-(α -naphthylmethyl)-benzoic acid with anhydrous zinc chloride at 180°. The material was found to be so unstable that purification was not feasible.

It seemed likely that the anthrone synthesis of Cook would be capable of wide application if the anthrone were available in a more satisfactory condition, and we consequently investigated this phase of the problem. The preparation of the 2-(α -naphthylmethyl)-benzoic acid required as starting material by the reduction of 2-(α -naphthoyl)-benzoic acid with zinc dust and alkali⁷ has been tried repeatedly in this Laboratory with disappointing results. Although with closely analogous keto acids reduction by this method usually proceeds very well, a product of satisfactory purity is obtained with the specific example at hand only after a tedious process of purification and in poor yield. A much better method was found in the high-pressure hydrogenation of the keto acid without solvent at 175° in the presence of copper chromite catalyst,⁸ a pure product being obtained in excellent yield after a single crystallization. No reduction occurred when solvent alcohol was employed. The 2-(α -naphthoyl)-benzoic acid was at first prepared by the Friedel and Crafts reaction, but the separation of the desired product from the β -isomer⁹ proved to be so tedious and wasteful that this was abandoned in favor of the Grignard condensation between phthalic anhydride and α -bromonaphthalene,¹⁰ which was found very satisfactory. On one occasion, when commercial α -bromonaphthalene was used without further purification, the keto acid obtained had the

correct melting point but failed to undergo hydrogenation even after repeated crystallization. The difficulty was traced to the reduction of the catalyst to the metallic condition under the influence of a trace of hydrogen bromide liberated from a small amount of bromonaphthoyl-benzoic acid present in the material prepared from halide contaminated with dibromonaphthalene.

Cook⁵ noted that sulfuric acid alone is not a satisfactory reagent for effecting the cyclization of 2-(α -naphthylmethyl)-benzoic acid since it leads to considerable oxidation and sulfonation. We found that these side reactions can be avoided to some extent by using a suitable diluent. Employing for the ring closure a mixture of sulfuric and phosphoric acids at room temperature, the crude anthrone was obtained in over 90% yield. This material, however, deteriorated badly on standing and extensive decomposition occurred on attempted crystallization. Submitted to reaction with methylmagnesium iodide or ethylmagnesium bromide, the crude products gave, after dehydration, some of the expected 10-methyl- and 10-ethyl-1,2-benzanthracene, but the yields were low and considerable unreacted material was recovered. This recovered product is quite easily purified and considerably less subject to decomposition than the starting material.

The pure, crystalline substance isolated in this way was found to be the enolic form of the compound, 1,2-benz-10-anthranol (III). It was subsequently established that the anthranol is not produced under the influence of the Grignard reagent but is present to a considerable extent in the crude product of cyclization and that addition occurs only to such of the keto-form as is contained in the material submitted to reaction. The stability in solvents of the recovered anthranol in contrast to the crude starting material suggested that a purification of the latter might be accomplished most effectively through some other functional derivative of the anthranol, such as the acetate. We were not able to prepare 1,2-benzanthranol-10-acetate (II) satisfactorily from the very sensitive anthrone-anthranol mixture resulting from cyclization with sulfuric-phosphoric acid, but found that some of this substance is produced, along with some 1,2-benz-10-anthrone (IV), when the acid I is warmed with a mixture of sulfuric and acetic acids. It seemed likely that under conditions more favorable to acetylation

(5) Cook, *J. Chem. Soc.*, 1087 (1930).

(5a) Cook, Robinson and Goulden, *ibid.*, 393 (1937).

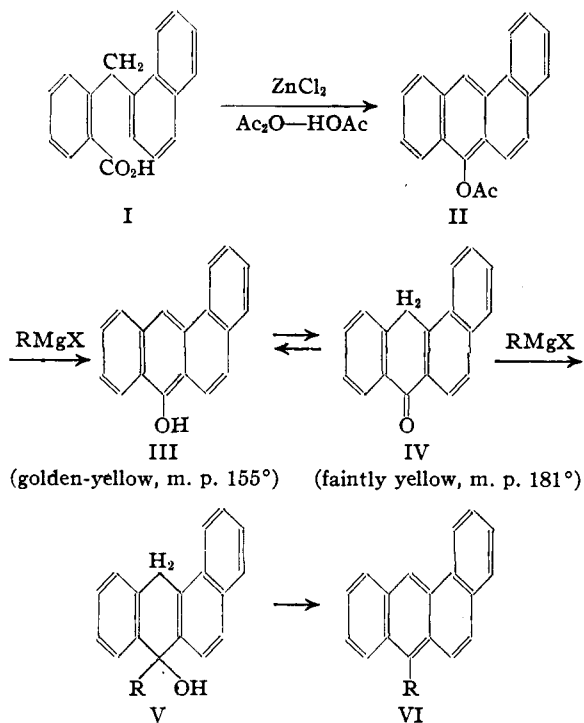
(6) Cook, *ibid.*, 456 (1932).

(7) Scholl, Seer and A. Zincke, *Monatsh.*, 41, 583 (1920).

(8) Connor, Folkers and Adkins, *THIS JOURNAL*, 54, 1138 (1932).

(9) Willstätter and Waldschmidt-Leitz, *Ber.*, 54, 1420 (1920).

(10) Weizmann, E. Bergmann and F. Bergmann, *J. Chem. Soc.*, 1367 (1935).



the tautomeric equilibrium would be displaced by the removal of the anthranol as the acetate, and various mixtures containing acetic anhydride were tried. Since zinc chloride in the molten state effects ring closure,⁵ we investigated the action of this substance in solution and eventually developed a method of cyclization which leaves little to be desired.

The new method consists in heating 2-(α -naphthylmethyl)benzoic acid (I) with about 0.1 molecular equivalent of zinc chloride in a mixture of acetic anhydride and acetic acid at the boiling point for about one hour. After adding water and cooling, 1,2-benzanthranol-10-acetate separates in a crystalline and completely pure condition in yield of about 90%. Zinc chloride in catalytic amounts also promotes cyclization in acetic anhydride solution alone, but the anhydride itself is attacked under these conditions with consequent darkening. This effect is eliminated by using some acetic acid as a diluent. Stannous chloride can be used also as the catalyst, but it does not seem to offer any advantages. The method of cyclization has been found applicable to some, if not all, other 2-arylmethylbenzoic acids, γ -arylbutyric acids, and β -arylpropionic acids thus far investigated; a study of additional examples is under way and will be reported separately.

The hydrolysis of the acetate II was accomplished very satisfactorily by treatment with excess Grignard reagent, the pure enolic tautomer III being obtained in over 80% yield. 1,2-Benz-10-anthranol forms bright golden yellow blades melting at 155°. The substance is completely stable in the solid state and it undergoes only very slow isomerization in most solvents. Acetone combines rapidly with the anthranol to give what appears to be a labile, colorless molecular compound and in the boiling solvent the enol form partially isomerizes at a moderately rapid rate to 1,2-benz-10-anthrone (IV), which was isolated in a pure condition by crystallization from acetone-ligroin after boiling the solution to effect a partial equilibration. This process could not be carried to completion, however, for solutions containing acetone suffer decomposition after refluxing for a few hours, apparently before equilibrium is established. The anthrone IV is a faintly yellow substance melting at 181°, and it is more soluble in hydrocarbon solvents than the anthranol III. Both tautomers can be crystallized without change from benzene or toluene if the heating is not prolonged, but when a toluene solution of the anthranol is refluxed for several hours partial isomerization to the anthrone occurs. Little decomposition takes place in hydrocarbon solvents, and this was the most satisfactory method found for obtaining the anthrone in a condition suitable for the Grignard reaction.

For the preparation of the methyl ether of 1,2-benz-10-anthranol, the usual process of methylation in alkaline solution did not appear practical because in such a medium the substance is rapidly oxidized by the air to the corresponding quinone. It was found that the ether can be obtained conveniently by cleaving the acetate II with a Grignard reagent and heating the resulting solution of the magnesium bromide salt with dimethyl sulfate.

From such general comparisons as can be made with K. H. Meyer's observations concerning the parent pair of tautomers, anthranol and anthrone,¹¹ it appears that the enol form is a somewhat more favored structure in the 1,2-benzanthracene series than with the anthracene compounds, as would be expected from theoretical considerations,¹² but until a direct comparison of

(11) K. H. Meyer, *Ann.*, **379**, 37 (1911); K. H. Meyer and Sander, *ibid.*, **396**, 133 (1913).

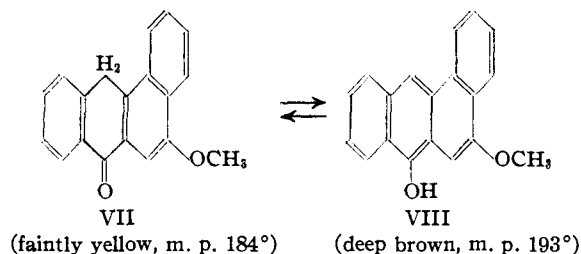
(12) Fieser and Lothrop, *This Journal*, **58**, 749 (1936).

the two systems can be made it is perhaps well to reserve judgment on this point.

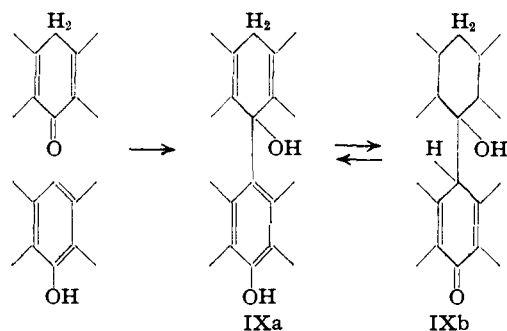
Having developed a good method of preparing pure 1,2-benz-10-anthranol and a reasonably satisfactory method of effecting its isomerization, little difficulty was experienced in synthesizing a series of 10-alkyl-1,2-benzanthracenes. In some instances crystallizates consisting wholly or largely of the keto form were employed for the Grignard reaction, but the best procedure consists in refluxing a solution of the anthranol in toluene for several hours and adding the cooled solution containing a large proportion of the anthrone to a solution of the Grignard reagent. Addition of the reagent proceeds rapidly and smoothly and moderate heating of the reaction product is sufficient to effect dehydration of the dihydroanthranol derivative (V). Some 1,2-benz-10-anthranol not originally isomerized usually can be recovered with ease in a satisfactory condition and traces of oxygen-containing compounds are eliminated readily by adsorption on alumina. Pure *n*-alkyl compounds were obtained in this way in average yield of about 50%. The 10-methyl-1,2-benzanthracene obtained was identical with the material synthesized by Fieser and Newman.² The 10-isopropyl compound was prepared for comparison with Cook's material⁶ and the properties were as reported. The yield in this preparation was poor and in one experiment the principal product isolated was a substance having the composition of a tetrahydro derivative of 10-isopropyl-1,2-benzanthracene; it yielded the latter hydrocarbon on dehydrogenation with sulfur. We plan to investigate this substance further and to study the reduction of 1,2-benzanthracene derivatives under other conditions. The more usual type of reduction, resulting in the formation of 1,2-benzanthracene, was observed to occur to an appreciable extent only in one instance. The series of 10-substituted derivatives prepared included the ethyl, *n*-propyl, *n*-butyl, *n*-amyl, and allyl compounds. 10-Allyl-1,2-benzanthracene is converted smoothly on hydrogenation into a hydrocarbon identical with the synthetic 10-*n*-propyl derivative.

A few 10-alkyl derivatives of the weakly carcinogenic¹³ 3-methoxy-1,2-benzanthracene also were prepared, and here the process proved to be considerably simpler. The pale yellow, crude

product resulting from the cyclization of 2-(4'-methoxy-1'-naphthylmethyl)-benzoic acid with cold sulfuric acid,¹⁴ although tending to decompose on attempted crystallization from most solvents,¹⁴ is less sensitive than the methoxyl-free material.



In each case cyclization with sulfuric acid seems to produce initially the keto form, which isomerizes to some extent when washed with water and undergoes slow change even on storage in the solid state. It was found that pure 3-methoxy-1,2-benz-10-anthrone (VII) can be obtained easily in fair yield by quickly crystallizing the crude, moist cyclization product from acetone. The anthranol, VIII, was first isolated in small amount from the mother liquor, and this tautomer later was prepared by the isomerization of the pure anthrone with boiling pyridine. There was isolated as a by-product in this reaction a high-melting, sparingly soluble, yellow compound having the composition of the starting material. This most likely is formed by the condensation of the enol and keto forms, giving the dianthranol-like substance IXa or the tautomer IXb. A similar substance was isolated as a by-product in the preparation of 10-*n*-amyl-1,2-benzanthracene and, since it is colorless, it probably has the ketonic structure IXb.



From the pure anthrone VII, the 10-methyl, 10-ethyl, and 10-*n*-propyl derivatives of 3-methoxy-1,2-benzanthracene were obtained in good yield by the Grignard synthesis.

(13) Fieser, Hershberg, Long, Jr., and Newman, *THIS JOURNAL*, **59**, 475 (1937).

(14) Fieser and Dietz, *ibid.*, **51**, 3141 (1929).

The 1,2-benzanthracene derivatives described in this paper are being tested for carcinogenic activity by Dr. M. J. Shear. The synthesis of 10-substituted compounds is being continued.

Experimental Part¹⁵

2-(α -Naphthoyl)-benzoic Acid.—Material prepared by the Friedel and Crafts reaction in tetrachloroethane solution at 10° and obtained in 84% yield after one crystallization, melted at 150–170° and afforded a pure product only after several recrystallizations and with heavy losses. In the large-scale preparation by the alternate method,¹⁶ 145 g. of carefully fractionated α -bromonaphthalene, b. p. 155.0–155.5° (25 mm.), m. p. 4–5°, was converted into the Grignard reagent in benzene (100 cc.)–ether (400 cc.) solution and this was added slowly to a vigorously stirred suspension of 111 g. of phthalic anhydride in 700 cc. of hot benzene. After stirring for two hours on the steam-bath, the mixture was worked up as usual and the product, collected after removing the solvent with steam, was mixed with soda solution and submitted to steam distillation. The dinaphthyl phthalide present remained undissolved, and after treating the solution with Norite at 10–15° the acid was precipitated, washed, drained well with the use of a rubber dam, and crystallized from an alcohol (500 cc.)–water (300 cc.) mixture; yield, 144 g. (75%); m. p. 174–176°.

2-(α -Naphthylmethyl)-benzoic Acid.—Reduction with zinc and alkali⁷ gave satisfactory material, m. p. 147–148°, in about 20% yield after several crystallizations from benzene–ligroin and methanol.

In a typical hydrogenation experiment 144 g. of the once crystallized, halogen-free keto acid and 8 g. of copper chromite catalyst (37 KAF⁸) were shaken with hydrogen at 2300–1500 lb. (156–102 atm.) pressure and 175° for two and one-half to three hours, when the reaction was complete. The temperature may be raised to 200° without ill effect. On cooling the bomb the product was found as a light green, crystalline cake. It was dissolved in a solution of 60 g. of sodium carbonate in 500 cc. of water by warming on the steam-bath and the solution was treated with Norite and poured into dilute hydrochloric acid. The collected and washed precipitate, crystallized while damp from 1500 cc. of methanol and 500 cc. of water, gave in the first crop 113 g. (82%) of colorless product, melting at 144–146° and suitable for cyclization. Only oily material was obtained from the mother liquor. The recrystallized acid formed flat needles, m. p. 148–148.5°.

Keto acid prepared by the Friedel and Crafts synthesis also was hydrogenated easily; with repeatedly recrystallized acid prepared from Eastman α -bromonaphthalene, b. p. 146–149° (16 mm.), the catalyst invariably was reduced to the metallic condition and the keto acid was recovered unchanged.

Cyclization of 2-(α -Naphthylmethyl)-benzoic Acid (I).

(a) **With Sulfuric-Phosphoric Acid.**—The finely powdered (ball mill) acid (25 g.) was added to a vigorously stirred mixture of 200 cc. of concentrated sulfuric acid and 400 cc. of sirupy phosphoric acid (85%) at 20–30° and after

two and one-half hours the deep red solution was filtered through sintered glass to remove unchanged acid (3.3 g.) and poured on cracked ice. The collected pale yellow precipitate was washed well with water and with dilute hydrochloric acid and dried in vacuum at room temperature; yield, 19.5 g. (94%); m. p. 130–135°.

This material deteriorates rapidly on standing; it is considerably less stable when washed with dilute soda solution, for this seems to promote isomerization to the enol form and secondary changes. Some isomerization probably occurs during the process of drying. Solutions of the acid-washed product darken rapidly, and attempted crystallizations were unsuccessful. In a typical Grignard reaction with freshly prepared material, 12 g. of the crude anthrone–anthranol mixture gave 2.25 g. of hydrocarbon and 5.5 g. of recovered 1,2-benz-10-anthranol, indicating the presence of at least 20% of keto form and 50% of enol form in the mixture.

(b) **With Sulfuric-Acetic Acid.**—A solution of 6 g. of the acid (I) in 70 cc. of glacial acetic acid was added to 90 cc. of concentrated sulfuric acid diluted with 20 cc. of glacial acetic acid, and after maintaining the mixture at 50–60° for twenty minutes it was poured on ice. The collected solid, washed with acetone and crystallized from this solvent, gave 2.3 g. of 1,2-benzanthranyl-10-acetate, m. p. 152–154°, together with some 1,2-benz-10-anthrone.

(c) **With Zinc Chloride as Catalyst.**—The most satisfactory procedure found was as follows. A mixture of 5 g. of 2-(α -naphthylmethyl)-benzoic acid, 30 cc. of glacial acetic acid, 20 cc. of acetic anhydride, and 0.4 g. of anhydrous zinc chloride was refluxed for one hour, during which time the solution acquired only a pale yellow color. Water was added cautiously under reflux in amount sufficient to produce a saturated solution, and on slow cooling very pure 1,2-benzanthranyl-10-acetate (II) separated in beautiful, colorless needles; yield, 4.95 g. (91%). The material softened at 161° and melted at 163–163.5°. Cook⁵ reports that the ("straw-colored") sample prepared by acetylation of the crude anthrone melted at 156° to a cloudy liquid becoming clear at 163°.

In earlier experiments, using as much as 75 g. of the acid I, the acetate was obtained in a slightly less pure condition in 70–80% yield on heating the acid for about one hour in acetic anhydride containing catalytic amounts of zinc chloride, stannous chloride, or a mixture of these halides. Acetic anhydride itself is attacked at the boiling point by these reagents, with considerable darkening, and when the undiluted anhydride was employed for cyclization the solution invariably turned dark brown. The acetate was brown and usually melted at about 153–156°; the melting point became constant at 162.5–163° only after seven crystallizations. Dilution with acetic acid eliminated this difficulty.

1,2-Benz-10-anthranol (III).—To effect cleavage, 16.1 g. of the acetate (II) was added to the Grignard reagent from 38 g. of *n*-butyl bromide, 150 cc. of benzene was added, the ether was allowed to distil, and the clear, deep orange to brown solution was refluxed for one hour. After treatment with dilute hydrochloric acid, the benzene layer was separated while hot, and on concentrating the solution a first crop of product (10.3 g.), m. p. 152–154°, and a second crop (1.3 g.), m. p. 148–150°, were obtained (yield,

(15) All melting points are corrected. Analyses by Mrs. G. M. Wellwood.

84%). On recrystallization from benzene the substance separated as rosetts of lustrous, golden yellow prismatic blades, m. p. 154.5–155.5°.

Anal. Calcd. for $C_{18}H_{12}O$: C, 88.49; H, 4.96. Found: C, 88.49; H, 4.85.

1,2-Benz-10-anthranol is readily soluble in glacial acetic acid or benzene and moderately soluble in alcohol; the solutions are only pale yellow in color and exhibit a blue fluorescence in ultraviolet light. The first two solvents are most satisfactory for crystallization. When the powdered anthranol is covered with a little acetone it sets to a cake, and on stirring the yellow substance rapidly changes to a colorless solid. This appears to be a labile molecular compound of the enol form, for when it was collected rapidly by centrifugation it turned yellow on drying and the melting point was that of the anthranol. The pure anthranol dissolves in dilute alkali very slowly in the cold but rapidly when warmed, yielding a yellow solution which on being shaken with air soon becomes cloudy, owing to the separation of the corresponding quinone (vat test).

1,2-Benz-10-anthranol was obtained also by refluxing the acetate (1 g.) with methanol (100 cc.) saturated with hydrogen chloride for fifteen hours. The product was precipitated with water and crystallized from benzene-ligroin, giving 0.5 g. of anthranol, m. p. 150–153°.

1,2-Benz-10-anthrone.—Isomerization of the anthranol seems to take place more rapidly in acetone than in other solvents, but secondary changes occur fairly soon in boiling acetone and considerable material is destroyed if refluxing is continued for more than a brief period. In isolated experiments the pure anthrone was obtained in about 50% yield by crystallization of the anthranol from dilute acetone, but the results were irregular and the material in the mother liquor was not recoverable. The keto form was isolated in yields of 20–25% by crystallization from acetone-ligroin, and by evaporating solutions of the anthranol in acetone at room temperature in vacuum.

Pure 1,2-benz-10-anthrone can be recrystallized without change from acetone or benzene and forms faintly yellow needles melting at 180–181°, dec.

Anal. Calcd. for $C_{18}H_{12}O$: C, 88.49; H, 4.96. Found: C, 88.34; H, 5.01.

The compound is insoluble in cold alkali but dissolves fairly readily on boiling to a yellow solution which soon becomes cloudy through oxidation. The anthrone is more soluble in hydrocarbon solvents than the anthranol and the solutions are colorless and non-fluorescent.

10-Methoxy-1,2-benzanthracene.—To the Grignard reagent from 3.84 g. of *n*-butyl bromide in ether, 2 g. of 1,2-benz-10-anthranol acetate was added. After refluxing for one hour, 7.1 g. of dimethyl sulfate was added in 50 cc. of toluene and the mixture was heated for four hours on the steam-bath, allowing the ether to distil. Water was added, the mixture was warmed and stirred for one hour on the steam-bath to decompose the excess reagent, and the washed toluene layer was diluted with benzene and passed through a tower of activated alumina, which removed some unmethylated anthranol. The filtrate was evaporated to dryness and the residue crystallized from benzene-ligroin, giving 1.0 g. (55%) of satisfactory material, m. p. 108–110°. The recrystallized ether formed colorless, diamond-shaped prisms, m. p. 110.5–111°.

Anal. Calcd. for $C_{19}H_{14}O$: C, 88.35; H, 5.47. Found: C, 88.19; H, 5.72.

10-Alkyl-1,2-benzanthracenes

In the most satisfactory procedure, a solution of pure 1,2-benz-10-anthranol in toluene was refluxed for twelve hours to effect partial isomerization and allowed to cool; the solution was decanted from crystals of anthranol which separated, this material was refluxed with fresh toluene for seven hours, and the two solutions were combined and added to the Grignard reagent. Yields of hydrocarbon up to 66% show that at least this proportion of the keto form is produced by this treatment. The keto form does not appear to suffer isomerization to any appreciable extent in the course of the reaction, for the yield of hydrocarbon (ethyl) from the pure anthrone was 82%. The Grignard reaction is rapid, and usually the mixture was decomposed after stirring and warming for about one hour on the steam-bath. The organic layer was separated and washed, and after removing the solvent by distillation the residue was heated for a few minutes on the hot-plate in order to effect the complete dehydration of the dihydroanthranol derivative (V). The material was then taken into benzene and the solution was allowed to cool. Some unchanged 1,2-benz-10-anthranol often crystallized at this point and could be recovered in a satisfactory condition. The anthranol can be separated very easily from the (very soluble) hydrocarbon present in the solution, but the recovered material was not employed for the preparation of a sample of a different hydrocarbon when this was to be used for biological experiments. This limitation does not apply to the preparation of the anthranol from its acetate, for here there is little chance of the formation of a hydrocarbon and the purification was more than adequate to remove possible traces of the very soluble *n*-butyl compound. Traces of the anthrone, anthranol, and other contaminants were removed very effectively by next passing the benzene solution through a tower of activated alumina, and the hydrocarbon was obtained in a very satisfactory condition from the filtrate.

The properties and analyses of the hydrocarbons and their picrates are given in the table. The hydrocarbons crystallize well from methanol or ethanol, as do the picrates. The hydrocarbons and their solutions show a brilliant blue fluorescence in ultraviolet light. 10-Methyl-1,2-benzanthracene, prepared only in a qualitative experiment from a crude anthrone-anthranol mixture, melted at 139–140° and gave no depression when mixed with the sample of Fieser and Newman.³ Additional details of individual experiments are recorded below. Where fractionation of a commercial sample of an alkyl halide was required, the boiling point of the material used is recorded.

Ethyl Compound.—A solution of 1.8 g. of pure 1,2-benz-10-anthrone, m. p. 180–181°, in 100 cc. of hot benzene was added slowly to the stirred Grignard reagent from 8.1 g. of ethyl bromide in 100 cc. of ether. After a transient red phase, the solution became light greenish-yellow; refluxing was continued for three hours. The yield of once crystallized (from alcohol) hydrocarbon, m. p. 112–113°, was 1.55 g. (82%).

***n*-Propyl Compound.**—Eight grams of 1,2-benz-10-anthranol was refluxed for twelve hours with 100 cc. of

toluene, the unchanged enol which crystallized on cooling was refluxed with 100 cc. of fresh toluene; the solutions were combined and added to the Grignard reagent from 3.9 g. of *n*-propyl chloride, b. p. 45.7–46.2°. On working up the mixture, 2.1 g. of 1,2-benz-10-anthranol was recovered and the first crop of *n*-propyl-1,2-benzanthracene from methanol melted at 100–102° and weighed 4.3 g. (66%, allowing for the recovery). The melting point was constant after four recrystallizations. The second crop of crystals (0.45 g.) consisted largely of 1,2-benzanthracene, which after further purification was identified by mixed melting point determination.

10-*i*-Propyl-1,2-benzanthracene and the Tetrahydro Derivative.—In the first experiment 4.5 g. of crude 1,2-benz-10-anthrone collected from several isomerization experiments was added in benzene solution to the Grignard reagent from 2 g. of magnesium and 6.5 g. of commercial isopropyl chloride (which on subsequent fractionation distilled at 34.9–35.0°). The ether was largely removed by distillation and the greenish-yellow solution was refluxed for five hours. The crude oily product crystallized only slowly; recrystallization from dilute acetic acid gave 2 g. of material, m. p. 71–73°, and 0.5 g., m. p. 69–71° (50%). On further crystallization from methanol the hydrocarbon formed iridescent, cream colored leaflets, m. p. 72.5–73.5°. The picrate separates as reddish-black, well-formed needles from methanol and melts at 134.5–135.5°. The analyses indicate that the hydrocarbon is a 10-*i*-propyltetrahydro-1,2-benzanthracene.

Anal. Calcd. for $C_{21}H_{22}$: C, 91.91; H, 8.10. Found: C, 92.00; H, 7.95. Picrate, calcd. for $C_{21}H_{22} \cdot C_6H_5O_7N_3$: C, 64.41; H, 5.00; N, 8.34. Found: C, 64.67; H, 4.81; N, 8.58.

10-ALKYL-1,2-BENZANTHRACENES

Alkyl group	M. p., °C.	Description	Analyses, %				M. p., °C.	Description	Analyses, %	
			Carbon		Hydrogen				Nitrogen	
			Calcd.	Found	Calcd.	Found		Calcd.	Found	
Ethyl	113.5–114	Faintly green-yellow needles	93.71	93.48	6.29	6.28	141–141.5	Dull red needles	8.66	8.49
<i>n</i> -Propyl	107–108	Colorless needles	93.80	93.01	6.70	6.97	126.5–127.5	Dull red needles	8.42	8.32
<i>i</i> -Propyl	93–93.5 ^a	Thick, pale yellow needles	93.80	93.13	6.70	6.79	159–160 ^b	Light reddish-brown needles	8.42	8.37
Allyl	125.5–126.5	Pale yellow needles	93.99	93.70	6.02	6.16	132–133	Deep red needles	8.45	8.44
<i>n</i> -Butyl	96.8–97.5	Silky, greenish fluorescent needles	92.89	93.04	7.11	6.95	115–115.5	Orange-red needles ^c	8.19	8.22
<i>n</i> -Amyl	82.5–83.5	Silky, greenish fluorescent needles	92.56	92.50	7.45	7.60	111–111.5	Dull red needles	7.97	7.95

^a Cook⁶ reports 94–95°. ^b Cook⁴ reports 157–158°. ^c About a twofold excess of picric acid is required in the crystallization of the picrate to prevent its dissociation.

Later observations suggest that the reduction to the tetrahydro compound may have occurred at an earlier stage in the process rather than in the Grignard reaction, and this possibility is being investigated further.

When the hydrocarbon (0.5 g.) was heated with selenium at 300–305° for ten hours, the extracted product crystallized from methanol as colorless plates (0.15 g.) melting at 157–159°. The melting point was raised to 159–160° on further purification, and the substance gave no depression when mixed with an authentic sample of pure 1,2-benzanthracene melting at the same temperature. The isopropyl group at the 10-position evidently is eliminated in the course of the high-temperature dehydrogenation, but when the tetrahydro compound (0.2 g.) was heated for one-half

hour with sulfur (50 mg.) at 240–245° the reaction product obtained melted at 93–93.5° and was found by mixed melting-point determination to be identical with the sample of 10-isopropyl-1,2-benzanthracene prepared as described below. The tetrahydro compound (0.2 g.), warmed in glacial acetic acid solution (5 cc.) with chromic anhydride (0.16 g.) in dilute acetic acid (2 cc.) for one and one-half hours, was converted into 1,2-benzanthraquinone (25 mg.), identified by comparison with an authentic sample.

In further experiments the Grignard reagents from redistilled isopropyl chloride (b. p. 34.9–35.0°) and from isopropyl bromide (b. p. 59.3–59.5°) were brought into reaction with crude 1,2-benz-10-anthrone under conditions very similar to those described above, but the only product isolated in a pure condition was 10-*i*-propyl-1,2-benzanthracene. In the experiment with the bromide there was obtained from 6 g. of the anthrone 2 g. of a crude hydrocarbon crystallize melting at about 58–62°. After five crystallizations from methanol, the 10-isopropyl compound was obtained in a satisfactory condition, m. p. 93–93.5° (0.8 g.). The results were similar in the second experiment with isopropyl chloride.

Allyl Compound.—1,2-Benz-10-anthranol was isomerized with toluene as above and treated with two equivalents of allylmagnesium bromide, prepared in 80% yield according to Gilman and McGlumphy.¹⁶ Once crystallized hydrocarbon, m. p. 117–122°, was obtained in 49% yield, and three crystallizations from ethyl alcohol gave a pure product. On hydrogenation in absolute alcoholic solution, using Adams catalyst, the allyl compound was converted into 10-*n*-propyl-1,2-benzanthracene, m. p. 106.5–107.5° (78% yield).

***n*-Butyl Compound.**—Using crude 1,2-benz-10-anthrone (3.45 g.) and *n*-butyl chloride (10.5 g.), b. p. 77.5–78.4°, the yield of crude hydrocarbon, m. p. 92–95°, was 2.25 g. (56%).

***n*-Amyl Compound.**—From 7.6 g. of the anthranol, isomerized with toluene, and 9.4 g. of *n*-amyl bromide, b. p. 127.5–128°, there was obtained 1 g. of a sparingly soluble condensation product, which crystallized from the toluene solution after concentration, and 3.4 g. (37%) of the hydrocarbon, m. p. 77–79° (a second crop of 1.2 g. (13%) melted at 65–70°). The pure hydrocarbon, obtained on three crystallizations from methanol, exhibits a brilliant bluish-green fluorescence even in daylight.

(16) Gilman and McGlumphy, *Bull. soc. chim.*, **43**, 1322 (1928).

The condensation product forms colorless needles from toluene and melts at 265–267°, dec. The composition is that of the anthrone and anthranol, and the properties are suggestive of a dimolecular, dianthrone-like structure (keto form of IX).

Anal. Calcd. for $C_{20}H_{16}O_2$: C, 88.49; H, 4.94. Found: C, 88.95, 88.89; H, 4.98, 5.11.

3-Methoxy-10-methyl-1,2-benzanthracenes

3-Methoxy-1,2-benz-10-anthrone (ol).—It was found expedient to conduct the cyclization of 2-(4'-methoxy-1'-naphthylmethyl)-benzoic acid (20 g.) at 3–5° rather than at 20°. The pale yellow precipitated material was drained well with the use of a rubber dam and divided into three portions. Each portion, while still moist, was dissolved quickly in hot acetone and the solution was rapidly concentrated until crystals began to form. The combined first crops, consisting chiefly of the anthrone, weighed 6.6 g. (35%) and melted at 170–175°. A second combined crop of 6.2 g. consisted of a mixture of the keto and enol forms, and some brown crystals of the anthranol could be separated mechanically with little difficulty.

After three crystallizations from acetone the anthrone melted constantly at 183–184° and formed long, silky, pale yellow needles. The substance is very soluble in benzene or glacial acetic acid and moderately soluble in acetone or alcohol. It is insoluble in cold, dilute alkali and hot alkali gives a yellow oil. The anthranol, obtained as above and also by the action of boiling pyridine on the pure ketone, crystallizes from glacial acetic acid as fan-shaped clusters of short, deep brown prisms melting at 192–193°. The anthranol is more soluble in hydroxylic solvents and acetone than the tautomer.

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 83.18; H, 5.15. Found (anthrone): C, 82.85; H, 5.24; (anthranol) C, 82.84; H, 5.50.

On isomerizing the anthrone with pyridine there was obtained in addition to the anthranol a sparingly soluble condensation product (probably IXa) which formed yellow needles from glacial acetic acid and melted with decomposition in the range 268–275°. When the capillary was inserted in a bath at 230°, the sample melted and resolidified without darkening, and melted with decomposition at 268–275°.

Anal. Calcd. for $C_{20}H_{16}O_4$: C, 83.18; H, 5.15. Found: C, 83.29; H, 5.02.

3-Methoxy-10-methyl-1,2-benzanthracene.—3-Methoxy-1,2-benz-10-anthrone (3.2 g., m. p. 179–181°) was added as a solid to the Grignard reagent from 4 g. of magnesium and methyl chloride in 150 cc. of ether, 100 cc. of benzene was added to the clear solution, the ether was distilled, and the solution was refluxed for three hours. After decomposition and separation of the layers, the benzene solution was evaporated, the residue was heated on the hot-plate to effect dehydration of the dihydroanthranol, and after passing a solution of the residue in benzene through a tower of alumina, the reaction product was obtained by concentrating the solution and adding ligroin; yield, 1.7 g. (53%); m. p. 182–183°. Recrystallization from alcohol and from benzene–ligroin gave slender, faintly yellow needles, m. p. 183–183.5°. The picrate,

when prepared in alcohol–benzene, formed brown needles, m. p. 141–143°, but it changed to orange-red needles, m. p. 149–150°, when recrystallized from benzene–ligroin. The compound contains two molecules of picric acid, one probably being associated with the hydrocarbon residue and the other with the ether group.

Anal. Calcd. for $C_{20}H_{16}O$: C, 88.20; H, 5.92. Found: C, 88.24; H, 6.34. Picrate, calcd. for $C_{20}H_{16}O \cdot 2C_6H_3O_7N_3$: N, 11.51. Found: N, 11.27.

3-Hydroxy-10-methyl-1,2-benzanthracene was prepared by refluxing the ether (0.5 g.) in glacial acetic acid (20 cc.) with 48% hydrobromic acid for one hour. The deep green solution deposited green needles on cooling. After recrystallizing the product twice from dilute acetic acid and once from benzene–ligroin, the hydroxy compound (0.2 g.) formed straw-colored, silky needles, m. p. 193–194°, dec. The compound is very soluble in alcohol or acetic acid and moderately soluble in benzene.

Anal. Calcd. for $C_{19}H_{14}O$: C, 88.35; H, 5.47. Found: C, 88.39; H, 5.71.

3-Methoxy-10-ethyl-1,2-benzanthracene, prepared as above, was obtained in a satisfactory condition in 67% yield. The substance crystallizes from benzene–alcohol as faintly yellow, diamond-shaped prisms, m. p. 161–161.5°. The picrate forms brick-red needles, m. p. 143.5–144°, from benzene–ligroin.

Anal. Calcd. for $C_{21}H_{18}O$: C, 88.01; H, 6.36. Found: C, 88.11; H, 6.52. Picrate, calcd. for $C_{21}H_{18}O \cdot 2C_6H_3O_7N_3$: N, 11.29. Found: N, 11.12.

3-Methoxy-10-n-propyl-1,2-benzanthracene.—Using *n*-propyl chloride, the yield of material, m. p. 134–135°, was 76%. After three crystallizations from benzene–alcohol, the compound formed nearly colorless needles, m. p. 136–136.5°. The picrate separated from benzene–ligroin as glistening, brick-red elongated plates, m. p. 140–140.5°.

Anal. Calcd. for $C_{22}H_{20}O$: C, 87.94; H, 6.73. Found: C, 87.77; H, 6.45. Picrate, calcd. for $C_{22}H_{20}O \cdot 2C_6H_3O_7N_3$: N, 11.11. Found: N, 11.35.

Summary

The preparation of a series of 10-alkyl-1,2-benzanthracenes, of interest in connection with the correlation of carcinogenic activity and structure, presented certain difficulties largely associated with the instability of the crude 1,2-benz-10-anthrone obtained by known methods of cyclization. The difficulty was overcome by the development of a new method of cyclization, using zinc chloride as a catalyst in acetic acid–anhydride solution, and yielding the anthranol acetate. Cleavage with a Grignard reagent gave the pure anthranol, and this was partially isomerized to the anthrone with boiling toluene. By the addition of Grignard reagents to the anthrone, and dehydration, the desired hydrocarbons were easily synthesized.

10-Alkyl derivatives of 3-methoxy-1,2-benzanthracene were obtained by a similar but

simpler process.

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The Heat Capacities of Selenium Crystals, Selenium Glass, and Tellurium at Low Temperatures¹

BY C. TRAVIS ANDERSON²

The data presented in this report represent a portion of an investigation being carried out at the Pacific Experiment Station of the U. S. Bureau of Mines on the possible specific heat anomalies of manganese selenide, and telluride, similar to those already found in the oxide³ and the sulfide.⁴

Since it was necessary to prepare pure selenium and tellurium to be used in this investigation, it was considered desirable to make low temperature specific heat measurements on these materials.

slightly above their melting points, the purification of the selenium was carried out in a glass apparatus while quartz was used for the tellurium. The samples were distilled a number of times, until no residue remained in the distilling flask or condensed material accumulated above the main body of distillate.

In preparing the samples, the glassy form of selenium was usually obtained in the distillation. To convert the glass to the crystals, the selenium was alternately warmed and cooled until the mass crystallized. The only detectable impurities found to be present were approximately 0.2% tellurium in the selenium and a similar amount of selenium in the tellurium. No corrections were made for these small amounts of impurities. Measurements were made on 261.3 g. of the selenium crystals, 237.4 g. of the selenium glass, and 374.2 g. of the tellurium.

The Specific Heats.—The results obtained in this Laboratory on the heat capacities of selenium crystals, selenium glass, and tellurium, expressed in gram calories (15°) per gram atomic weight, are shown graphically in Fig. 1. The experimental values for the heat capacities are given in Tables I, II, and III. The calculations were made on the basis of Se = 78.96 and Te = 127.61.

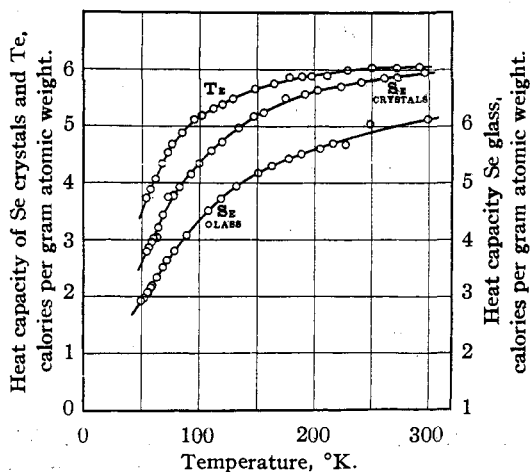


Fig. 1.—The heat capacity of selenium crystals, selenium glass and tellurium, in calories per gram atomic weight.

Materials.—The tellurium used in this investigation was furnished through the courtesy of Mr. J. O. Betterton of the American Smelting and Refining Co. The sample of selenium was of regular c. p. quality.

Both the selenium and tellurium were purified further by vacuum distillation. At temperatures

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(3) Millar, *THIS JOURNAL*, **50**, 1875 (1928).

(4) Anderson, *ibid.*, **53**, 476 (1931).

TABLE I
HEAT CAPACITY PER GRAM ATOMIC WEIGHT OF SELENIUM
CRYSTALS

T, °K.	C _p	T, °K.	C _p	T, °K.	C _p
54.4	2.786	77.7	3.772	155.4	5.236
56.1	2.864	82.8	3.920	174.5	5.494
58.7	2.956	92.4	4.149	191.5	5.562
60.1	3.018	99.5	4.342	202.7	5.633
63.4	3.035	110.0	4.566	223.2	5.702
64.6	3.211	119.3	4.724	240.9	5.776
68.3	3.428	133.9	4.974	261.2	5.850
72.9	3.746	147.0	5.166	272.7	5.861
77.6	3.773			296.5	5.952