[CONTRIBUTION FROM THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY]

Preparation of Polycyclic Aromatic Hydrocarbons as Potential Carcinogens[1]

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RECEIVED DECEMBER 3, 1952

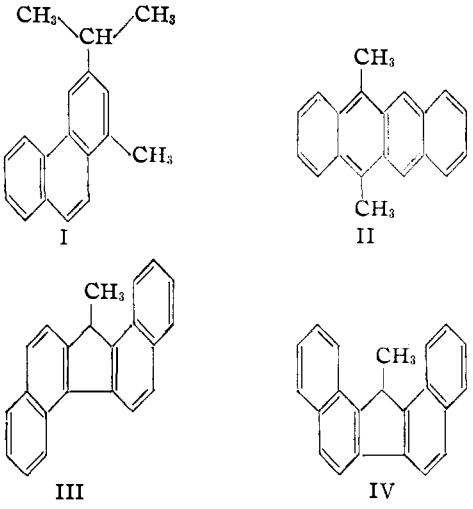
In order to test a hypothesis which postulates certain features of the phenanthrene ring system to be essential for hydrocarbon carcinogens, the following two hydrocarbons were synthesized: 1-methyl-3-isopropylphenanthrene by a route involving the Pschorr reaction; 6,11-dimethylnaphthacene *via* hydroxynaphthacenequinone. An apparently general method for the preparation of 9-alkyl dibenzfluorenes was found through isomerization of dinaphthylethylenes, and 9-methyl-1,2,5,6- and 9-methyl-1,2,7,8-dibenzfluorene were synthesized.

Many hypotheses have been advanced to account for the unique properties of certain polycyclic aromatic hydrocarbons in producing tumor growth. The fact that most of the compounds in this class contain the phenanthrene ring system substituted by condensed aromatic rings and methyl groups, has led to the idea that some feature of this system may be necessary for and involved in the carcinogenic process. In particular, the 9,10-bond of phenanthrene, activated by substitution in the phenanthrene ring system, may be an active part of the carcinogen molecule.[3] 1-Methyl-3-isopropylphenanthrene (I) was prepared to test this hypothesis, since this hydrocarbon consists of the phenanthrene ring system substituted in such a way as to result in an activation of the 9,10-bond.

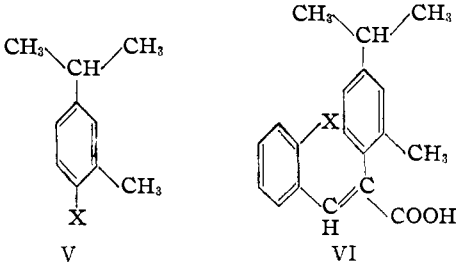
The potent carcinogen 9,10-dimethyl-1,2-benzanthracene contains the activated phenanthrene ring system; it seemed of interest to ascertain whether a hydrocarbon which retains the substituted, condensed four rings of this compound, but lacks the phenanthrene system, would correspondingly be devoid of carcinogenic activity. 6,11-Dimethylnaphthacene (II) was synthesized as it fulfills these structural requirements. Since methyl substitution in positions 9 and 10 of the benzanthracene series greatly enhances carcinogenicity, the effect of 9-methyl substitution in the weak carcinogens 1,2,5,6-dibenzfluorene and 1,2,7,8-dibenzfluorene were investigated (III) and (IV). These compounds bear a spatial rather than chemical resemblance to the corresponding carcinogens in the benzanthracene series (1,2,5,6- and 1,2,7,8-dibenzanthracene) and thus the spatial effect of a substituted methyl group could be tested. While this work was in progress, a synthesis of III by a different method was published.[4]

Preliminary tests were carried out by Dr. I. Berenblum,[5] who found 1-methyl-3-isopropylphenanthrene (I) to be very weakly carcinogenic and 9-methyl-1,2,5,6- and 9-methyl-1,2,7,8-dibenzfluorene (III and IV) to be non-carcinogenic. 6,11-Dimethylnaphthacene (II) was too unstable for biological tests.

A synthesis of 1-methyl-3-isopropylphenanthrene (I) has been reported,[6] although no experimental details were given. For the purpose of the present synthesis of the compound, *m*-cymene (V, X = H),



prepared from fenchone,[7] was chloromethylated. The constitution of 1-chloromethyl-2-methyl-4-isopropylbenzene (V, X = CH_2Cl) was established by reduction to the known compound 1,2-dimethyl-4-isopropylbenzene (V, X = CH_3) with zinc dust in glacial acetic acid. For comparison this compound (V, X = CH_3) was prepared from carvone.[8] In addition, the chloromethyl compound was transformed into *m*-cymenealdehyde (V, X = CHO) by treatment with hexamethylenetetramine. The semicarbazone of this aldehyde was shown to be identical with that of *m*-cymenealdehyde obtained from *m*-cymene by the Gattermann–Koch reaction.[9] The aldehyde was reduced by the Clemmensen method to dimethylisopropylbenzene (V, X = CH_3) identical with that obtained by reduction of the chloromethyl compound (V, X = CH_2Cl).



The chloromethyl compound (V, X = CH_2Cl) was transformed into the cyanomethyl compound which upon hydrolysis afforded 2-methyl-4-isopropylphenylacetic acid. This was condensed

(1) This work was submitted in partial fulfillment of the requirements of the Doctor of Philosophy degree at Oxford University.

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(3) C. L. Hewett, *J. Chem. Soc.*, 299 (1951); G. N. Badger, *Brit. J. Cancer*, **2**, 309 (1948).

(4) J. W. Cook and R. W. G. Preston, *J. Chem. Soc.*, 553 (1944).

(5) *24th Annual Report, Brit. Empire Cancer Campaign*, 126 (1947).

(6) G. Darzens and A. Levy, *Comp. rend.*, **201**, 152 (1935).

(7) D. Wallach, *Ann.*, **275**, 157 (1893).

(8) A. Klages and F. Sommer, *Ber.*, **39**, 2306 (1906).

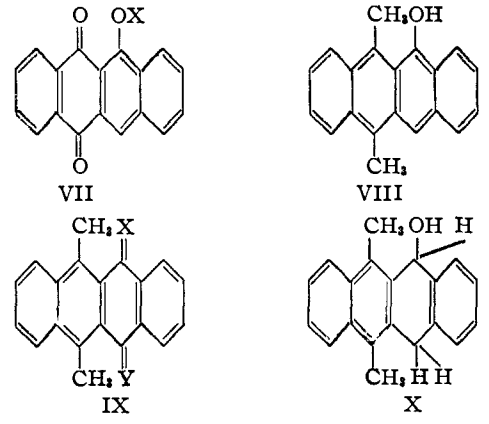
(9) P. Chuit and J. Bolle, *Bull. soc. chim.*, [4] **35**, 200 (1924).

with *o*-nitrobenzaldehyde. Since the by-product in this reaction, *o*-nitrocinnamic acid, is sparingly soluble in ether, *o*-nitro-α-2′-methyl-4′-isopropylphenylcinnamic acid (VI, X = NO_2) was purified by extraction with that solvent. The compound was readily reduced to *o*-amino-α-2′-methyl-4′-isopropylphenylcinnamic acid (VI, X = NH_2) by ferrous sulfate and ammonia. Cyclization to 1-methyl-3-isopropyl-10-phenanthroic acid was carried out by the method of Pschorr.[10] The resulting mixture of the phenanthroic acid and a by-product, probably *o*-hydroxymethylisopropylphenylcinnamic acid, was treated with hydrogen chloride in methanol. It was assumed that the phenolic acid would be more easily esterified than the phenanthroic acid.[11] The latter was then extracted as the sodium salt. After regeneration, the phenanthroic acid was decarboxylated to give 1-methyl-3-isopropylphenanthrene (I), corresponding in all properties with those reported for it by Darzens and Levy.[6]

For the synthesis of 6,11-dimethylnaphthacene (II), *o*-(1-hydroxy-2-naphthoyl)-benzoic acid,[12] was cyclized to 5-hydroxynaphthacene-6,11-quinone (VII, X = H),[13] which was methylated to VII (X = CH_3) with methyl sulfate in boiling nitrobenzene in presence of potassium carbonate.[14] 5-Hydroxy-6,11-dimethylnaphthacene (VIII), existing in acidic or neutral solution as the anthrone, 6,11-dimethyl-5-oxo-12-hydronaphthacene (IX, X = O, Y = H_2), was obtained by treatment of the methoxyquinone (VII, X = CH_3) with methylmagnesium iodide according to the method described by Hershberg and Fieser.[15] The Grignard adduct of the quinone was decomposed by hydriodic acid, affording an intermediate compound thought to be 6-iodomethyl-11-methyl-5-oxo-12-hydronaphthacene. The Grignard reagent appears to act here also as a demethylating agent on the methoxyl group. The unstable iodomethyl compound was reduced to the anthrone (IX, X = O, Y = H_2) by stannous chloride.

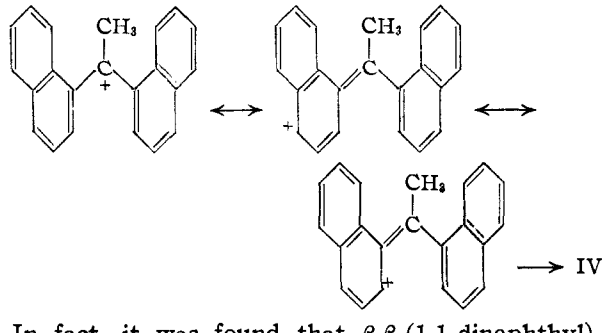
The anthrone (IX, X = O, Y = H_2) is changed to the anthranol (VIII) by treatment with alcoholic alkali, whereupon a green color appears. The anthrone is not affected by aqueous alkali because of the stability of the anthrone form. The anthranol (VIII) was readily reduced by zinc dust in alcoholic alkali to the dihydroanthranol, 6,11-dimethyl-5-hydroxy-5,12-dihydronaphthacene (X). The dihydroanthranol loses the elements of water very easily, on heating or by treatment with mineral acids, to form the hydrocarbon, 6,11-dimethylnaphthacene (II). However, the hydrocarbon could not be obtained in a pure state from X, since contamination with a photo-oxide inevitably took place. The photo-oxide formed with excessive ease from the hydrocarbon in presence of atmospheric oxygen and light.

(10) R. Pschorr, *Ber.*, **29**, 496 (1896).
(11) *Cf.* C. L. Hewett and R. H. Martin, *J. Chem. Soc.*, 1396 (1940).
(12) C. Deichler and C. Weizmann, *Ber.*, **36**, 719 (1903).
(13) I. Y. Postovskii and L. N. Goldyrev, *J. Gen. Chem. U.S.S.R.*, **11**, 429 (1941).
(14) R. Robinson, E. N. Hindmarsh and I. Knight, *J. Chem. Soc.*, 940 (1917).
(15) E. B. Hershberg and L. F. Fieser, THIS JOURNAL, **63**, 2561 (1941).



Eventually, the pure hydrocarbon was obtained in the following way. 6,11-Dimethylnaphthacene-5,12-quinone (IX, X = Y = O) was prepared by oxidation of the anthrone (IX, X = O, Y = H_2). It is very stable and gives the vat-test color only with alcoholic alkali. When reduced by zinc dust in alcoholic alkali, 6,11-dimethyl-5,12-dihydronaphthacene (IX, X = Y = H_2) was obtained. When more dilute alkali was used in this reduction, the dihydroanthranol (X) could be isolated, which shows this compound to be an intermediate in the reduction of the quinone to the dihydrocompound. On heating dimethyldihydronaphthacene (IX, X = Y = H_2) with copper bronze in an inert atmosphere *in vacuo*[16] dimethylnaphthacene (II) sublimed and was recrystallized in an inert atmosphere. When a solution of the hydrocarbon is exposed to both light and air, it loses its yellow color and green fluorescence and the photo-oxide is obtained. On heating, the photo-oxide decomposes to give a dimethylnaphthacenequinone which is different from 6,11-dimethylnaphthacene-5,12-quinone (IX, X = Y = O).

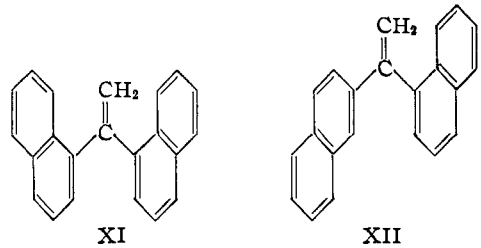
An apparently general method for the preparation of 9-alkyl dibenzfluorenes was found through an isomerization of dinaphthylethylenes. Consideration of the reaction mechanism of the cyclodehydration method for the preparation of fluorene derivatives, led to the conclusion that the dinaphthylethylenes might react in a similar way. In response to an electrophilic reagent, a carbonium ion stabilized by resonance would be formed, which could cyclize to produce the fluorene derivative.



In fact, it was found that β,β-(1,1-dinaphthyl)-ethylene[17] (XI) isomerized and cyclized to 9-methyl-1,2,7,8-dibenzfluorene (IV) by treatment

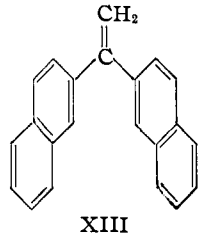
(16) *Cf.* E. Clar, *Ber.*, **72**, 1817 (1939).
(17) P. Pfeiffer and P. Schneider, *J. prakt. Chem.*, **129**, 129 (1931).

with anhydrous aluminum chloride or stannic chloride. The ultraviolet spectrum of the methyldibenzfluorene was almost identical with that of the known 1,2,7,8-dibenzfluorene, except for a slight shift to the ultraviolet. The fluorescence spectra were identical.



XI

XII



XIII

β,β-(1,2′-Dinaphthyl)-ethylene (XII) prepared by a reaction of 2-naphthylmagnesium bromide with 1-acetonaphthenone,[18] afforded, under similar conditions, 9-methyl-1,2,5,6-dibenzfluorene (III), although the yield in this case was lower. Its spectrum was again found to be almost identical with that of 1,2,5,6-dibenzfluorene. Its physical properties were in good agreement with those reported by Cook and Preston.[4]

β,β-(2,2′-Dinaphthyl)-ethylene (XIII), prepared by treatment of 2-naphthylmagnesium bromide with ethyl acetate, could not be isomerized to the corresponding methyldibenzfluorene, but appeared to give a dimer.

Acknowledgment.—The author is deeply indebted to Professor Sir Robert Robinson for his generous help and advice throughout the course of this work.

Experimental

Chloromethylation of *m*-Cymene.—Anhydrous hydrogen chloride was passed into a suspension of paraformaldehyde (4 g.) in glacial acetic acid (50 ml.) for 30 minutes with cooling in ice, until a clear solution was obtained. *m*-Cymene[7] (V, X = H) (15 g.) was added and the mixture shaken at room temperature for 24 hours. The resulting solution was poured into water, extracted with ether and the extract washed with sodium carbonate solution and dried. 1-Chloromethyl-2-methyl-4-isopropylbenzene (V, X = CH_2Cl) distilled at 134° (16 mm.) (yield 9.6 g., 52%) after evaporation of the solvent, the residual, nearly theoretical quantity of *m*-cymene being recovered in the fraction of the distillate boiling below 90°.

1,2-Dimethyl-4-isopropylbenzene (V, X = CH_3).—(a) 1-Chloromethyl-2-methyl-4-isopropylbenzene (2 g.) was dissolved in glacial acetic acid (20 ml.) and boiled, while zinc dust (6 g.) was added in small portions for 30 minutes. The solution was then cooled, poured into water, extracted with ether, the extract washed with sodium carbonate solution and after evaporation of the solvent, 1,2-dimethyl-4-isopropylbenzene distilled at 83° (15 mm.), $n^{21}D$ 1.5000 (b.p. and refractive index identical with those given by Klages and Sommer[8]).

This hydrocarbon (0.5 g.) was poured into chlorosulfonic acid (2 g.) with stirring and cooling of the solution to −5°. The solution was then kept at 0° for 12 hours. The sulfonyl chloride of the hydrocarbon was obtained by pouring the solution onto ice and collecting the solid by filtration. It was dissolved in hot aniline and the solid sulfonanilide of 1,2-dimethyl-4-isopropylbenzene was collected after removing the excess aniline by shaking with dilute hydrochloric acid. The compound crystallized from alcohol in colorless needles, m.p. 186°.

(b) Zinc filings (8.5 g.), after being left in contact with a 10% solution of mercuric chloride for 1 hour and washed by decantation with dilute hydrochloric acid, were covered with concentrated hydrochloric acid and *m*-cymenealdehyde (V, X = CHO) (to be described below) (1 g.). The mixture was boiled with frequent additions of concentrated hydrochloric acid, until most of the metal had dissolved, filtered and the hydrocarbon, after extraction from the filtrate with ether and distillation, was converted into the sulfonanilide as under (a).

Melting points of the sulfonanilide obtained from the hydrocarbon prepared by methods (a) and (b) were identical with the melting point of the sulfonanilide of the hydrocarbon prepared from carvone by the method of Klages and Sommer,[8] 186°. Melting points of specimens of sulfonanilide obtained by methods (a) and (b), when mixed with a specimen prepared by the method of Klages and Sommer, or when mixed with one another, showed no depression.

2-Methyl-4-isopropylbenzaldehyde (*m*-Cymenealdehyde) (V, X = CHO).—(a) To a solution of 1-chloromethyl-2-methyl-4-isopropylbenzene (7 g.) in glacial acetic acid at the boiling point, was added hexamethylenetetramine (5.4 g.). Boiling was continued for a further 30 seconds, the solution was cooled, water added (50 ml.) and the aldehyde extracted with ether. The extract was washed with sodium carbonate solution, dried and, after evaporation of the solvent, the aldehyde was shaken with a saturated solution of sodium metabisulfite. The bisulfite compound of the aldehyde which precipitated was washed with ether and decomposed by a solution of sodium carbonate. *m*-Cymenealdehyde could be distilled, as a colorless liquid (3 g. or 49%), at 130° (11 mm.).

(b) Anhydrous hydrogen chloride and carbon monoxide were passed, with continuous stirring, into a flask containing *m*-cymene (20 g.), anhydrous cuprous chloride (2.1 g.) and anhydrous aluminum chloride (18.5 g.). The carbon monoxide was passed in at a rate twice as great as that of the hydrogen chloride. The reaction mixture was kept at 20° for the first hour, at 30° for the following 5 hours and finally poured onto ice and steam distilled. The distillate was extracted with ether and purified in the same way as the aldehyde obtained from the chloromethyl compound. The yield was low.

When treated with semicarbazide hydrochloride, the aldehyde obtained both from the chloromethyl compound and from *m*-cymene itself gave the same semicarbazone which crystallized from alcohol in colorless, short rods, m.p. 206°, alone and mixed with one another. Chuit and Bolle[9] give a m.p. 199°.

Anal. Calcd. for $C_{12}H_{17}ON_3$: C, 64.9; H, 7.8. Found: C, 64.9; H, 7.5.

***o*-Nitro-α-2′-methyl-4′-isopropylphenylcinnamic Acid** (VI, X = NO_2).—1-Chloromethyl-2-methyl-4-isopropylbenzene (39 g.), dissolved in acetone (440 ml.) and water (80 ml.), was refluxed with potassium cyanide (39 g.) for 12 hours, the acetone was evaporated, the residue extracted with ether and 1-cyanomethyl-2-methyl-4-isopropylbenzene was distilled as a colorless liquid at 156–157° (15 mm.), yield 33 g. or 91%. Hydrolysis of the nitrile (33 g.) in alcohol (35 ml.) and water (24 ml.) with potassium hydroxide (33 g.) was complete in 20 hours. The acid was precipitated by adding dilute hydrochloric acid and after dissolving in sodium carbonate solution and reprecipitating with acid, 2-methyl-4-isopropylphenylacetic acid, m.p. 82°, was obtained after recrystallization from boiling alcohol (37.5 g. or 96%).

Potassium 2-methyl-4-isopropylphenylacetate (prepared by dissolving potassium (6.18 g.) in anhydrous alcohol (60 ml.) with cooling, adding methylisopropylphenylacetic acid (30.5 g.) and evaporating the alcohol *in vacuo*), redistilled acetic anhydride (162 g.) and a drop of pyridine, were mixed and *o*-nitrobenzaldehyde (24 g.) was added slowly. The mixture was heated, first at 120° for 2 hours without condenser, then at 100° for 24 hours. The resulting solution

(18) N. Froeschl and J. Harlass, *Monatsh.*, **59**, 275 (1932).

was poured into water, the acetic anhydride decomposed by gently warming and the product dissolved in ether. Some *o*-nitrocinnamic acid, which formed as a by-product, was separated by filtration, being sparingly soluble in ether. The nitro acid was then extracted by a solution of sodium carbonate which was filtered and acidified. The product was purified through its ammonium salt which is sparingly soluble in water. The nitro acid crystallized from xylene in cream-colored needles, m.p. 195°, yield 24.9 g. or 46%.

Anal. Calcd. for $C_{19}H_{19}O_4N$: C, 70.1; H, 5.9. Found: C, 69.6; H, 6.0.

o-Amino-α-2'-methyl-4'-isopropylphenylcinnamic Acid (VI, X = NH_2).—The nitro acid (16 g.) in aqueous ammonia (d. = 0.88, 75 ml.) was heated at 100° with ferrous sulfate (150 g.) in water (375 ml.) for 2 hours. The black sludge was then filtered, the filtrate shaken vigorously to precipitate colloidal ferrous hydroxide and filtered again. The collected precipitates and filter papers were extracted with 1% ammonia solution until no more amino acid remained behind. The combined extracts and the filtrate were made acid to litmus, and thus precipitated, by acetic acid. The amino acid (9 g. or 65%) was purified through its sparingly soluble sodium salt, affording, after recrystallization from xylene, bright yellow needles, m.p. 185°.

Anal. Calcd. for $C_{19}H_{21}O_2N$: C, 77.3; H, 7.2. Found: C, 77.2; H, 6.7.

1-Methyl-3-isopropylphenanthrene (I).—The amino acid (5 g.), sodium carbonate (2.5 g.) and sodium nitrite (1.2 g.) were dissolved in hot water (25 ml.), cooled and added in small quantities and with vigorous stirring to a 6 *N* solution of sulfuric acid (110 ml.) at −10°, simultaneously with copper powder (6 g.). The latter was freshly prepared by precipitation by zinc dust from a solution of copper sulfate. The mixture was stirred at 0° for 1 hour and at room temperature for a further hour, until a drop of it showed no more purple color with an alcoholic solution of α-naphthylamine. The mixture was then filtered, the precipitate collected, dissolved in sodium carbonate solution and filtered again. The phenanthroic acid was precipitated from the filtrate together with a by-product, presumably hydroxymethylisopropylphenylcinnamic acid, by the addition of dilute hydrochloric acid. The mixture of acids was collected and dissolved in methanol. This solution was treated with dry hydrogen chloride to saturation and refluxed for 1 hour. The solution was then poured into water, extracted with ether and re-extracted with sodium carbonate solution from which the less easily esterified methylisopropylphenanthroic acid (2.8 g. or 61%) was regenerated.

The phenanthroic acid (2 g.) in quinoline (20 ml.) was heated to 250° for 1 hour with copper bronze (1 g.). The cooled mixture was filtered, the precipitate washed with ether and the quinoline extracted by shaking with successive quantities of dilute hydrochloric acid. The remaining ethereal solution was dried, evaporated, and the residue dissolved in a mixture consisting of 80 parts of ligroin and 20 parts benzene and passed through a column of alumina. The least strongly adsorbed band, which showed strong blue fluorescence in ultraviolet light, was collected, distilled at 133–136° (0.1 mm.) and crystallized from alcohol affording 1-methyl-3-isopropylphenanthrene (0.35 g. or 21% yield) in colorless, long needles, m.p. 79°. Darzens and Levy[8] report the same melting point.

Anal. Calcd. for $C_{18}H_{18}$: C, 92.2; H, 7.7. Found: C, 92.0; H, 7.7.

During chromatography a deep-blue liquid was isolated with the hydrocarbon fraction, which distilled at the same temperature. It could only be removed by crystallization of the hydrocarbon. Its nature could not be identified.

Methylisopropylphenanthrene formed an orange-colored picrate, m.p. 150°, identical in its properties with that described by Darzens and Levy.[8]

5-Methoxynaphthacene-6,11-quinone (VII, X = CH_3).—*o*-(1-Hydroxy-2-naphthoyl)-benzoic acid[12] (20 g.) was ground with boric acid (20 g.) and the mixture heated to 140–150° with concentrated sulfuric acid (40 ml.) for 3 hours. The precipitate, obtained by pouring the mixture into a large quantity of water, was collected and dissolved in a boiling solution of 2 *N* sodium hydroxide. The hot solution was filtered and the deep-red sodium derivative of hydroxynaphthacenequinone crystallized on cooling. The substance was collected by filtration, treated with dilute hydrochloric acid until orange-yellow, dried and recrystallized from xylene; yield 15.1 g. or 81%.

A suspension of hydroxynaphthacenequinone (10 g.) and anhydrous potassium carbonate (34 g.) in a mixture of nitrobenzene (50 ml.) and methyl sulfate (22.1 g.) was refluxed for 30 minutes. The nitrobenzene and methyl sulfate were removed by steam distillation and the resulting solid material collected by filtration. After drying, it was crystallized from boiling alcohol with a little benzene added. 5-Methoxynaphthacene-6,11-quinone (8.5 g. or 90%) crystallized in long, thin, yellow needles, which after recrystallization, gave a m.p. 210°.

Anal. Calcd. for $C_{19}H_{12}O_3$: C, 79.2; H, 4.2. Found: C, 79.6; H, 4.3.

The compound is soluble in alcohol and benzene, more so than the hydroxyquinone. It is stable to aqueous potassium hydroxide, but is quickly hydrolyzed by alcoholic alkali to the pink potassium derivative of the hydroxyquinone. With concentrated sulfuric acid it gives the permanganate-purple color characteristic of the quinonoid type of naphthacene derivative.

6,11-Dimethyl-5-*oxo*-12-hydronaphthacene (IX, X = O, Y = H_2).—5-Methoxynaphthacenequinone (28 g.), finely powdered, was added with stirring to a boiling Grignard solution consisting of magnesium (21 g.), methyl iodide (125 g.), ether (250 ml.) and benzene (450 ml.). The solution was stirred and boiled under reflux for 3 hours. The temperature of the purple solution was brought to 75° by evaporation of some ether. At the end of the specified time, the solution was cooled to −10° and the Grignard compound decomposed by adding a mixture of hydriodic acid (sp. gr. 1.7, 322 ml.) and acetic acid (350 ml.) with stirring. The benzene and ether were then evaporated under reduced pressure at room temperature. With quantities considerably smaller than those here described, it was possible to evaporate all the benzene and ether in a relatively short time. The compound thought to be 6-methyl-11-iodomethyl-5-oxo-12-hydronaphthacene then crystallized in large dark-brown plates which were collected, washed on the filter funnel with a dilute solution of acetic acid, dissolved in the reducing solution described below, and boiled for 30 minutes. When dealing with quantities as large as those here described, the benzene and ether were evaporated only until a viscous oil remained, floating on the hydriodic acid–acetic acid layer. The upper layer was separated, washed with dilute acetic acid and added to a reducing solution consisting of stannous chloride (200 g.), concentrated hydrochloric acid (400 ml.) and dioxane (450 ml.). A large quantity of water was added to the hydriodic acid–acetic acid layer, whereupon more iodomethyl compound precipitated. It was collected, washed with dilute acetic acid and also added to the above reducing solution. The reducing mixture, in two layers, was refluxed for 3 hours. When reduction was complete, the upper layer was separated and evaporated to dryness on the steam-bath under reduced pressure. More of the reaction product was obtained by adding water to the dioxane–hydrochloric acid layer and collecting the solid precipitate. The combined solid material was dissolved in benzene. The solution was purified by passing it through a column of alumina. The reaction product, 6,11-dimethyl-5-oxo-12-hydronaphthacene is less strongly adsorbed than the residual hydroxynaphthacenequinone and therefore is eluted first by the eluant, a mixture of benzene with a small quantity of alcohol. The anthrone appeared pink on the column and yellow in solution. Hydroxynaphthacenequinone appeared as a deep-orange band at the top of the column. The eluted benzene solution of the anthrone was concentrated and, if left overnight, crystallized in large orange cubes (13.8 g. or 52%). On recrystallization from a mixture of benzene and alcohol, the compound was obtained in long, thin, lemon-yellow needles, m.p. 179°.

Anal. Calcd. for $C_{20}H_{16}O$: C, 88.2; H, 5.9. Found: C, 87.7; H, 5.8.

The anthrone is readily soluble in benzene and sparingly soluble in alcohol and acetic acid. It is unaffected by aqueous potassium hydroxide, but dissolves in alcoholic potassium hydroxide to give a dark-green solution, which oxidizes in air to give a yellow solution of 6,11-dimethylnaphthacene-5,12-quinone, to be described below.

The compound gives the characteristic purple color with concentrated sulfuric acid.

6,11-Dimethyl-5-hydroxy-5,12-dihydronaphthacene (X).—The anthrone (IX, X = O, Y = H_2) (1 g.) and zinc dust (4.5 g.) were added to a mixture of sodium hydroxide (2 *N* solution, 30 ml.), toluene (10 ml.) and alcoholic potassium hydroxide (*N* solution, 20 ml.) and refluxed for 1 hour. The solution was cooled and extracted with benzene several times, the collected extracts were evaporated to dryness in presence of a drop of pyridine, dissolved in benzene with a drop of pyridine and rapidly chromatographed through a short column of alumina. Least strongly adsorbed was some 6,11-dimethylnaphthacene (II), giving a yellow solution with green fluorescence. The eluate was run directly into a receiver containing a few drops of a saturated solution of picric acid in alcohol, with which the hydrocarbon combined to give a solution of the black picrate. Higher on the column appeared a narrow buff-colored band which was eluted with benzene with a drop of alcohol added. On evaporation of the solvent from this fraction in presence of a drop of pyridine, a colorless solid was obtained (0.7 g.), which after recrystallization from a mixture of alcohol and benzene in presence of a trace of pyridine, gave a m.p. (with decomposition) 253°.

Anal. Calcd. for $C_{20}H_{18}O$: C, 87.5; H, 6.6. Found: C, 87.1; H, 5.9.

6,11-Dimethyl-5-hydroxy-5,12-dihydronaphthacene is soluble in benzene and sparingly soluble in alcohol. It loses the elements of water on heating or in presence of mineral acids, or merely by standing dissolved in a neutral solvent, to give dimethylnaphthacene, described below. With concentrated sulfuric acid it gives the dark-green color characteristic of dimethylnaphthacene.

6,11-Dimethylnaphthacene-5,12-quinone (IX, X = Y = O).—The anthrone (IX, X = O, Y = H_2) (1 g.) was suspended in propionic acid (40 ml.), potassium dichromate (1.4 g.) was added as well as water (0.2 ml.) and the solution refluxed for 8 hours. The solution was then poured into water, the precipitate collected, dried and dissolved in benzene. This solution was passed through a column of alumina. The quinone was less strongly adsorbed than any residual anthrone and passed through the column first, as a broad yellow band. On evaporation of the solvent from the eluate, the quinone crystallized (0.7 g.) and was recrystallized from alcohol affording short, lemon-yellow needles, m.p. 223°.

Anal. Calcd. for $C_{20}H_{14}O_2$: C, 83.9; H, 4.9. Found: C, 83.8; H, 5.0.

Dimethylnaphthacenequinone is readily soluble in benzene and soluble in alcohol. It gives the characteristic purple color with concentrated sulfuric acid. It is not reduced by stannous chloride in hydrochloric acid and remains unaffected by aqueous alkaline reducing agents (sodium hydrosulfite). It gives a vat-color with alcoholic alkaline sodium hydrosulfite, however.

6,11-Dimethyl-5,12-dihydronaphthacene (IX, X = Y = H_2).—Dimethylnaphthacenequinone (2 g.), alcohol (200 ml.), sodium hydroxide (30% aqueous solution) (20 ml.) and zinc dust (10 g.) were refluxed for 1 hour. The color of the solution changed from yellow (quinone) to purple (sodium derivative of the hydroquinone) to green to colorless (dihydro compound). The hot solution was filtered, the residue extracted repeatedly with boiling alcohol, and the collected extracts and the filtrate treated with water. The hydrocarbon (1.6 g. or 89%) precipitated and was recrystallized from boiling alcohol. It was obtained in long, colorless, lustrous needles, m.p. 126.5°.

Anal. Calcd. for $C_{20}H_{18}$: C, 93.0; H, 7.0. Found: C, 92.9; H, 7.2.

The hydrocarbon is readily soluble in alcohol, ether and benzene and gives the characteristic green color with concentrated sulfuric acid.

From a saturated solution of picric acid and dimethyldihydronaphthacene, the picrate crystallized in orange-red rods, m.p. 154°.

Anal. Calcd. for $C_{26}H_{21}O_7N_3$: C, 64.0; H, 4.4. Found: C, 63.5; H, 4.5.

When using a 10% solution of sodium hydroxide instead of a 30% solution in the reduction of dimethylnaphthacenequinone, the dihydroanthranol (X) could be isolated after 1 hour. The complete reduction took 8 hours.

6,11-Dimethylnaphthacene (II).—This hydrocarbon was obtained in a state of purity, free from contamination with photo-oxide, by the following method: dimethyldihydronaphthacene (0.1 g.) was thoroughly mixed with copper bronze (1 g.) and the mixture heated to 300° *in vacuo* in an inert atmosphere. 6,11-Dimethylnaphthacene sublimed and was collected. It was dissolved in alcohol under nitrogen and crystallized under nitrogen. It appeared in short, deep-orange needles, m.p. 183–184° (0.03 g.).

Anal. Calcd. for $C_{20}H_{16}$: C, 93.6; H, 6.2. Found: C, 93.0; H, 6.0.

Dimethylnaphthacene is readily soluble in benzene, soluble in alcohol and gives the characteristic green color with concentrated sulfuric acid. It forms a picrate crystallizing in short, black needles, m.p. 160–162°. The picrate was unstable in solution in absence of an excess of picric acid.

Dimethylnaphthacene, when exposed to light in a solution of carbon bisulfide with a stream of air bubbling through, rapidly changes into the photo-oxide, indicated by loss of the yellow color and green fluorescence of the solution. The color and fluorescence are retained if a solution of the hydrocarbon is kept in the dark or, alternatively, in light in a sealed tube in the absence of oxygen.

The photo-oxide was purified by precipitation by alcohol from a solution in benzene. It crystallized with one molecule of alcohol in colorless, microscopic, short rods, m.p. 245°, with decomposition beginning at 215°.

Anal. Calcd. for $C_{20}H_{16}O_2 \cdot C_2H_6O$: C, 79.0; H, 6.5. Found: C, 79.5; H, 5.6.

The compound gives the characteristic green color with concentrated sulfuric acid.

When the photo-oxide was heated in a sublimation apparatus, it decomposed at 230–270° (0.2 mm.) with evolution of some oxygen and sublimation of a purple solid. This compound was crystallized from alcohol and obtained in long, purple needles, m.p. 233°.

Anal. Calcd. for $C_{20}H_{14}O_2$: C, 83.9; H, 4.9. Found: C, 83.6; H, 4.7.

When dissolved in alcoholic potassium hydroxide in presence of sodium hydrosulfite and a drop of water, the purple solution of this compound changed to brilliant green. When shaken in air, it turned purple again, showing that the compound is a dimethylnaphthacenequinone, reduced to the hydroquinone by alcoholic alkaline reducing agents and re-oxidized to the quinone by air. A mixed melting point determination showed it to be different from the yellow 6,11-dimethylnaphthacene-5,12-quinone already described.

β,β-(2,2′-Dinaphthyl)-ethylene (XIII).—2-Iodonaphthalene (7.8 g.) in anhydrous ether (150 ml.) was added dropwise over a period of 1 hour to magnesium turnings (0.75 g.) in ether (5 ml.). The reaction was started by adding a drop of methyl iodide to the mixture. Anhydrous ethyl acetate (3.6 ml.) was added slowly with stirring and cooling to the Grignard mixture. The mixture was then refluxed for 4 hours, decomposed with ice and dilute hydrochloric acid and, after separation of the ethereal layer and evaporation of the solvent, the resulting oil was distilled at 195–200° (0.4 mm.) and crystallized from alcohol. Some 2,2′-dinaphthyl precipitated first and β,β-(2,2′-dinaphthyl)-ethylene, being more soluble in alcohol, then crystallized. On recrystallization it was obtained in colorless prisms, m.p. 100°.

Anal. Calcd. for $C_{22}H_{16}$: C, 94.2; H, 5.7. Found: C, 94.0; H, 5.7.

The hydrocarbon is readily soluble in benzene and light petroleum. With *s*-trinitrobenzene it forms a complex, crystallizing in yellow needles, m.p. 106°.

β,β-(1,2′-Dinaphthyl)-ethylene (XII).—2-Bromonaphthalene (2.7 g.) in anhydrous ether (30 ml.) was added slowly and dropwise over a period of 30 minutes to magnesium turnings (0.32 g.) in ether (5 ml.). If the bromonaphthalene is added too rapidly, large amounts of 2,2′-dinaphthyl are formed. The reaction was started by adding a drop of methyl iodide to the mixture. The mixture was then refluxed until all the magnesium was dissolved (1 hour). 1-Acetonaphthenone[18] (2.3 g.) in ether (15 ml.) was added slowly with cooling and stirring. The resulting solution was refluxed for 5 hours, cooled, decomposed by ice and dilute hydrochloric acid, the solvent was evaporated and the residual oil distilled. The first fraction, boiling below 140° (0.3 mm.) was unreacted ketone. Dinaphthylethylene distilled at 204° (0.3 mm.) (2.5 g. or 68%). It solidified upon standing at room temperature for several days, m.p. 73–74°.

Anal. Calcd. for $C_{22}H_{16}$: C, 94.2; H, 5.7. Found: C, 94.4; H, 5.7.

The compound forms a yellow picrate, m.p. 125°.

9-Methyl-1,2,7,8-dibenzfluorene (IV).—β,β-(1,1'-Dinaphthyl)-ethylene[17] (1 g.) was thoroughly mixed with anhydrous stannic chloride (1 g.). The complex, which formed readily, was a viscous gum of dark-green color. The mixture was stirred at room temperature for 2 minutes whereupon it turned brown. The complex was at once decomposed by the addition of dilute hydrochloric acid. The hydrocarbon was taken up in ether and the extract was shaken with more dilute acid to remove all stannic chloride. After evaporation of the solvent, the hydrocarbon (0.82 g.) crystallized from the solution. It was purified by dissolving in a saturated alcoholic solution of picric acid, from which deep-red needles of the picrate, m.p. 151°, were obtained. The picrate was recrystallized several times from alcohol in presence of some excess of picric acid and decomposed by passing an alcoholic solution of it through a column of alumina. The colorless solid obtained from the eluate was sublimed at 160° (0.1 mm.). The sublimate, 9-methyl-1,2,7,8-dibenzfluorene crystallized from ligroin in large, lustrous plates, m.p. 173°.

Anal. Calcd. for $C_{22}H_{16}$: C, 94.2; H, 5.7. Found: C, 93.9; H, 5.7.

The compound turns deep-green in concentrated sulfuric acid. With *s*-trinitrobenzene it forms a di-*s*-trinitrobenzoate which crystallized from alcohol in presence of some excess of trinitrobenzene and was obtained in clusters of yellow needles, m.p. 154°.

Anal. Calcd. for $C_{34}H_{22}O_{16}N_6$: C, 58.2; H, 3.1; N, 11.9. Found: C, 58.7; H, 3.1; N, 11.8.

9-Methyl-1,2,5,6-dibenzfluorene (III).—To β,β-(1,2'-dinaphthyl)-ethylene (1.3 g.) was added anhydrous stannic chloride (0.75 g.) and the resulting oily mixture stirred vigorously for 1 minute, while the color changed from deep-green to deep-purple. The complex was then decomposed by dilute hydrochloric acid, the hydrocarbon taken up in ether and shaken with more acid, the solvent partially removed and alcohol added. An amorphous, colorless solid precipitated from the solution, presumably a polymer of dinaphthylethylene. This compound could not be crystallized or sublimed; it did not form a complex with picric acid. It was removed by filtration and from the filtrate was obtained 9-methyl-1,2,5,6-dibenzfluorene (0.8 g. or 62%). This compound was purified by recrystallization of the deep-red picrate, m.p. 148°, which was decomposed by passing its alcoholic solution through a column of alumina. The solid obtained from the eluate was sublimed at 120° (0.3 mm.). The sublimate, after crystallization from alcohol, was obtained in colorless plates, m.p. 144° (Cook and Preston[4] report a m.p. 144–145°).

Anal. Calcd. for $C_{22}H_{16}$: C, 94.2; H, 5.7. Found: C, 94.2; H, 5.5.

Dimerization.—β,β-(2,2'-Dinaphthyl)-ethylene (1 g.), when mixed with anhydrous stannic chloride (1 g.) for 1 minute at room temperature, and decomposed with dilute hydrochloric acid, extracted with ether, washed with acid and precipitated with alcohol, gave a colorless, amorphous powder, which could be reprecipitated by alcohol from a solution in benzene, giving a m.p. 165–169°.

Anal. Calcd. for $C_{44}H_{32}$: C, 94.2; H, 5.7; mol. wt., 560. Found: C, 93.9; H, 5.8; mol. wt., 521.

The hydrocarbon is soluble in benzene, sparingly soluble in alcohol and ether and does not sublime when heated *in vacuo*. It does not form a complex with picric acid or *s*-trinitrobenzene.

OXFORD, ENGLAND

[CONTRIBUTION FROM ELECTROCHEMICALS DEPARTMENT, E. I. DU PONT DE NEMOURS & CO., INC.]

The Reactions of Vinyl Acetate with Aliphatic Hydroxy Compounds. A New Synthesis of Vinyl Ethers[1]

BY ROBERT L. ADELMAN

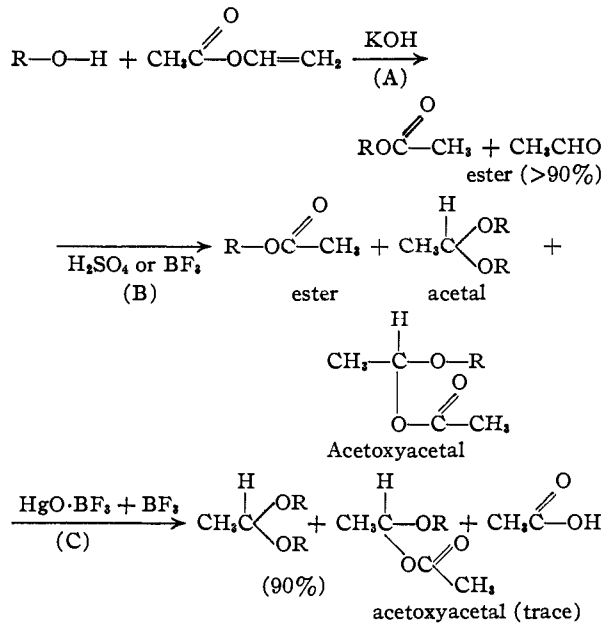
RECEIVED NOVEMBER 25, 1952

A new reaction of vinyl acetate with primary hydroxy compounds is described. At low temperatures in the presence of mercuric salts of strong acids, vinyl ethers and acetic acid are formed. A mechanism is suggested for this reaction which postulates that vinyl acetate dissociates to give an acetylene–mercury complex and acetic acid. This mechanism satisfactorily accounts for other mercuric salt-catalyzed reactions of vinyl acetate and alcohols.

The known reactions of vinyl acetate with aliphatic hydroxy compounds may be summarized as follows: (A) In the presence of alkaline catalysts, vinyl acetate is known to be an acetylating agent for aliphatic hydroxy compounds.[2] (B) With strong acids as catalysts, mixtures of acetals and transesterification products are formed in low conversions.[3] (C) With strong acids plus mercuric salts of strong acids as catalysts, the conversions and yields of acetals from primary aliphatic alcohols are markedly improved[3,4] and traces of acetoxyacetals are also produced.

The acetoxyacetal was postulated as the intermediate to acetal formation.[3]

Our findings demonstrate that when the reaction of primary aliphatic alcohols and vinyl acetate is



(1) This work was presented at the Atlantic City Meeting of the American Chemical Society, September, 1952. See also U.S.P. 2,579,411.

(2) V. L. Hansley, U. S. Patent 2,342,612 (1944); 2,355,971 (1944).

(3) W. J. Croxall, F. J. Glavis and H. T. Neher, THIS JOURNAL, **70**, 2805 (1948).

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