CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ALBERTA, AND THE CHEMICAL LABORATORIES OF HARVARD UNIVERSITY]

1,2,9,10-Tetramethylanthracene

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The study of model compounds structurally related to some of the more powerfully active carcinogenic hydrocarbons has suggested certain possible correlations between structure and carcinogenic activity. 1,2,9,10-Tetramethylanthracene has been considered of interest as a model of the highly active carcinogen 9,10-dimethyl-1,2-benzanthracene,[1] but all syntheses hitherto attempted have been unsuccessful. Badger, Cook and Goulden[2] succeeded in adding methyl Grignard reagent to 1,2-dimethylanthraquinone but found the dimethyl ether of the resulting diol resistant to normal reductive cleavage with sodium. Fieser and Webber[3] attempted a synthesis from a tetrahydro derivative of 1,2-dimethylanthraquinone but were unable to isolate a dimethyl diol derivative from the Grignard reaction. Badger, Gould and Warren[4] investigated the reduction of 1,2,9,10-tetramethyl-9,10-dihydroanthracene-9,10-diol with hydriodic acid in acetic acid solution but obtained only an amorphous product; when red phosphorus was added there resulted a dihydroanthracene derivative from which no product of dehydrogenation could be isolated.

In the present work a trial was made of the synthetic method developed by Sandin and Fieser.[5] The di-magnesio halide derivative resulting from the addition of methylmagnesium iodide to 1,2-dimethylanthraquinone (I) did not respond satisfactorily to treatment with hydriodic acid in the simple manner found applicable in the case of 1,2-benzanthraquinone, but on adjustment of the solvent mixture and by employing a mixture of hydriodic and hydrobromic acids a halogenated, oxygen-free reaction product was isolated in good yield; the reason for the beneficial action of hydrobromic acid is not known. The amorphous yellow substance proved too sensitive to be purified, but the halogen content was not far from that calculated for an iodomethyltrimethylanthracene, and the halogen was found by analysis to be essentially iodine rather than bromine. In analogy with the previous work,[5] the substance probably has the structure III, or is a mixture of III and IV. The iodo compound on interaction with sodium methoxide gave a mixture of two isomeric methoxy derivatives of the probable structures V and VI, which could be separated by fractional crystallization. One isomer (m. p. 125°) is regarded as the trimethylmethoxymethylanthracene V because of its yellow color and the blue fluorescence of its alcoholic solutions and because the substance forms a characteristic trinitrobenzene derivative. The second isomer (m. p. 142°) is colorless, non-fluorescent, and forms no complex with trinitrobenzene, and it is therefore regarded as the methylenedihydroanthracene VI. This substance is isomerized to V under the catalytic influence of hydrochloric acid. The two ethers may correspond to other transannular systems.[6]

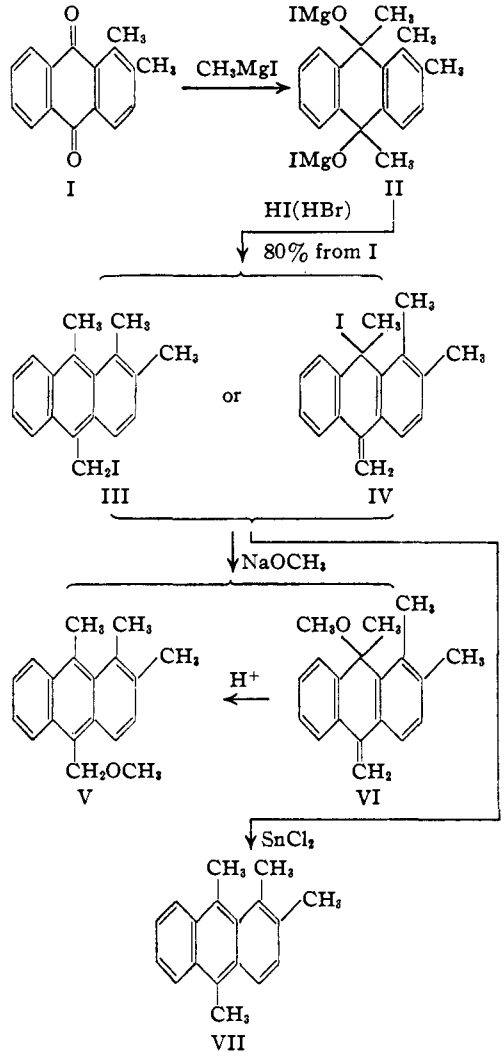
The iodo compound is readily reduced by stannous chloride in dioxane–hydrochloric acid, but the resulting hydrocarbon (VII) is extremely sensitive and is destroyed by brief exposure to air in contact with the acid reduction mixture. By rapid extraction with benzene and treatment of the fluorescent but oily product in alcoholic solution with picric acid, the substance was isolated in satisfactory yield as a black picrate, and the trinitrobenzene derivative was obtained similarly as purple needles. 1,2,9,10-Tetramethylanthracene was obtained by cleaving the picrate with ammonia and rapidly evaporating a benzene extract at room temperature. The hydrocarbon becomes oxygenated after brief periods of storage in the solid state. Facilities have not been available for tests of carcinogenicity.

Acknowledgment.—We are indebted to the Rockefeller Foundation for grants (to R. B. S.) in support of this and related work. We are also grateful to the Carnegie Corporation Research Grant of the University of Alberta for the purchase of equipment.

Experimental Part[7]

1,2-Dimethylanthraquinone of assured homogeneity was prepared from samples of 3-nitro-*o*-xylene kindly

(1) Bachmann and Chemerda, THIS JOURNAL, **60**, 1023 (1938).
(2) Badger, Cook and Goulden, *J. Chem. Soc.*, 16 (1940).
(3) Fieser and Webber, THIS JOURNAL, **62**, 1360 (1940).
(4) Badger, Gould and Warren, *J. Chem. Soc.*, 18 (1941).
(5) Sandin and Fieser, THIS JOURNAL, **62**, 3098 (1940).
(6) Cook, *J. Chem. Soc.*, 2798 (1928).
(7) Microanalyses by Eleanor Werble. All melting points are corrected.



supplied by Dr. R. T. Major, Merck and Company, Incorporated, and prepared according to Emerson and Smith[8] and distilled in vacuum through a 20-cm. Widmer column. The amine obtained on reduction[9] was crystallized as the formyl derivative[2] and converted through the bromide[2] to *o*-(2,3-dimethylbenzoyl)-benzoic acid.[2,8] The keto acid was cyclized by treatment with concentrated sulfuric acid at 60–70° for three hours; the quinone when crystallized from acetic acid melted at 157.5–158.5°.

Iodo Compound (III ?).—To a solution of the Grignard reagent from 0.5 g. of magnesium and excess methyl iodide in 20 cc. of anhydrous ether was added 0.5 g. of 1,2-dimethylanthraquinone. The flask was stoppered and after standing overnight at room temperature the fluorescent solution was poured dropwise and with constant stirring into a solution (cooled to 0°) of 7.5 cc. of 50% hydriodic acid and 5 cc. of hydrobromic acid (sp. gr. 1.4) in 20 cc. of methanol. Glacial acetic acid (20 cc.) was then added. The iodo compound separated as a yellow amorphous solid; yield, 0.6 g. The substance could not be purified and the sample analyzed was merely air-dried.

Anal. Calcd. for $C_{18}H_{17}I$: I, 35.25. Found: I, 32.70; 33.20.

A 0.3500-g. sample of silver iodide from the above determination was treated with chlorine and changed to silver chloride; the weight of chloride was 0.2160 g., in comparison with the calculated value 0.2132 g.

Yellow Methoxy Compound (V ?).—A 1.5-g. sample of the iodo compound was added to a solution of 3 g. of sodium methoxide in 50 cc. of absolute methanol. The iodide disappeared after heating at 60–70° for a short time, and dilution with water then afforded a solid which on crystallization from methanol was found to be a mixture of two compounds. These could be separated mechanically, or by fractionation from methanol. One isomer was obtained as yellow needles, m. p. 124.5–125.5° (0.3 g.); the solutions in alcohol show a strong bluish fluorescence in daylight.

Anal. Calcd. for $C_{19}H_{20}O$: C, 86.32; H, 7.63. Found: C, 86.04; H, 7.63.

The **trinitrobenzene derivative** crystallized from alcohol in red needles, m. p. 142.5–143.5°.

Anal. Calcd. for $C_{19}H_{20}O \cdot C_6H_3O_6N_3$: C, 62.89; H, 4.86. Found: C, 63.28; H, 4.62.

White Methoxy Compound (VI ?).—The second component of the above reaction mixture was obtained as white needles, m. p. 141–142° (0.12 g.).

Anal. Calcd. for $C_{19}H_{20}O$: C, 86.32; H, 7.63. Found: C, 86.48; H, 7.81.

The substance dissolves in alcohol to give a non-fluorescent solution, and no coloration or separation of a complex is observed on the addition of trinitrobenzene. When a drop of hydrochloric acid is added to a solution of the white compound in methanol, marked fluorescence develops, and the addition of trinitrobenzene then results in the prompt separation of red crystals of the complex of the isomer V.

1,2,9,10-Tetramethylanthracene (VII).—A solution of 1.2 g. of the iodo compound in 60 cc. of dioxane was added to a solution of 10 g. of stannous chloride crystals in 50 cc. of dioxane and 15 cc. of concentrated hydrochloric acid. The solution was brought to its boiling point, diluted with 500 cc. of water and immediately extracted with benzene. The highly fluorescent benzene extract was washed with water as quickly as possible, and dried by filtering through ordinary filter paper. Evaporation of the benzene at room temperature in vacuum left a brown sirupy liquid which would not solidify. It was, therefore, extracted with a small amount of 95% ethanol, and the extract then saturated with picric acid. On slow cooling the black crystalline **picrate** of the hydrocarbon separated. Two to three crystallizations from 95% ethanol afforded 0.6 g. of beautiful, jet-black, slender needles, m. p. 137–138°.

Anal. Calcd. for $C_{18}H_{18} \cdot C_6H_3O_7N_3$: C, 62.20; H, 4.57. Found: C, 62.51; H, 4.72.

In a similar manner the **trinitrobenzene** derivative was prepared. It crystallized from 95% ethanol in purple needles, m. p. 170.5–171.5°.

Anal. Calcd. for $C_{18}H_{18} \cdot C_6H_3O_6N_3$: C, 64.42; H, 4.73 Found: C, 64.77; H, 4.42.

(8) Emerson and Smith, THIS JOURNAL, **62**, 141 (1940).
(9) Yokoyama, *Helv. Chim. Acta*, **12**, 771 (1929).

An attempt to recover the hydrocarbon from the picrate by means of activated alumina and super-cel was unsuccessful. The process finally adopted was to decompose a benzene solution of the picrate at room temperature with dilute ammonium hydroxide. The benzene extract was washed, dried, and evaporated *in vacuo* at room temperature, as rapidly as possible. This afforded a yellow solid, m. p. 52–54° with preliminary shrinkage and softening.

Anal.[10] Calcd. for $C_{18}H_{18}$: C, 92.26; H, 7.74. Found: C, 91.94; H, 7.84.

Subsequent analyses[10] at Alberta gave slightly lower carbon values (C, 91.46, 91.39; H, 7.64, 7.73). The sample having the analysis reported above when analyzed ten days later at Harvard gave values indicating the absorption of oxygen (C, 88.79, 88.93; H, 7.64, 7.83). The deteriorated sample melted unsharply at 80°, and gas was evolved at a temperature of 120°; the fluorescence in solution was markedly diminished. Attempts to crystallize fresh samples of the hydrocarbon from dilute acetic acid, 95% ethanol, benzene or petroleum ether were unsuccessful. Once the hydrocarbon was obtained as long yellow needles, m. p. 47–50°, from an alcoholic solution of the picrate treated with ammonium hydroxide. Attempts to purify these crystals further by the use of alumina resulted in the loss of the material.

(10) Semi-microanalyses performed by one of us (R. K.), N. M. Perkins and J. C. Nichol.

Summary

1,2,9,10-Tetramethylanthracene, of interest as a model of a potent carcinogen, has been synthesized and characterized in the form of the picrate, trinitrobenzene complex, and two methoxy derivatives. The hydrocarbon is very sensitive to air.

EDMONTON, ALBERTA
CAMBRIDGE, MASSACHUSETTS RECEIVED JULY 13, 1943

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE OHIO STATE UNIVERSITY]

Hydrogenation of the Triple Bond[1]

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Monoalkylacetylenes, treated with sodium in liquid ammonia, are one-third hydrogenated to the corresponding olefins, and two-thirds metalated. Dialkylacetylenes are reduced to the *trans* olefins whose physical properties are markedly different from those of the olefin obtained by catalytic hydrogenation. The latter have been labeled as *cis* compounds and claimed to be pure by Campbell and Eby.[2]

We have found that monoalkylacetylenes can be reduced quantitatively by the theoretical amount of sodium in liquid ammonia containing an ammonium salt, and that no hydrogen escapes. Under the same circumstances, dialkyl acetylenes are inefficiently reduced, hydrogen is evolved, and more than the theoretical amount of sodium is consumed. Ammonium chloride, which is appreciably soluble in liquid ammonia, gives off some hydrogen and causes an inefficient reduction in every case, while ammonium sulfate, which is nearly insoluble, proved almost 100% efficient in the reduction of monoalkylacetylenes. From these results, it is deduced that the hydrogen released from the acetylene molecule is more effective for reduction than the hydrogen from the ammonium ion, and that the function of the ammonium salt is to regenerate the acetylene from its sodium derivative.

A similar mechanism might be proposed for the reduction of dialkyl acetylenes, if the assumption is accepted that hydrogen on the carbon atoms adjacent to the triple bond has become acidic enough to react with sodium. This, however, is ruled out by the inefficiency of the reduction in the presence of ammonium sulfate. The formation of a disodium derivative of dialkyl acetylenes by addition of sodium to the triple bond seems more plausible; if this is accepted, a simple explanation can be given[3] for the formation of the *trans* olefin exclusively on the basis of repulsion between electrical charges. In contrast, when a triple bond is reduced to a double bond on a catalyst the mechanism consists merely in the breakage of one of the bonds with automatic set-up of the *cis* configuration, so long as molecular hydrogen only is involved.

Monoalkylacetylenes

I. Hydrogenation with Sodium Alone

(a) **Propyne.**—To 5 moles of sodium acetylide in two liters of ammonia was added 5 moles of dimethyl sulfate,

(1) The detailed preparation of acetylenic compounds in better yields and purity than recorded in the literature has been submitted to the Editor of *Industrial and Engineering Chemistry*. Practical directions for making sodium amide and sodium acetylide efficiently and handling them safely are described by us in "Inorganic Syntheses," Vol. II (in press), John Wiley and Sons, Inc., New York, N. Y.

(2) Campbell and Eby, THIS JOURNAL, **63**, 216, 2683 (1941).

(3) Greenlee and Fernelius, *ibid.*, **64**, 2505 (1942).