serve merely to establish that in a reaction which does not involve the hindered carbon the rates are comparable. No explanation is obvious for the fact that the *cis meso* isomer reacts somewhat more rapidly.

These experiments will be extended to other temperatures and the mechanisms of the reactions will be examined more closely when more material is available.

Summary

The rates of the acid-catalyzed esterification with methanol of the stereoisomeric 2,5-dimethylcyclopentanecarboxylic acids, the acid-catalyzed hydrolysis of the corresponding methyl esters, and the reaction of the sodium salts with phenacyl bromide were measured at 40°. The isomer believed to be the *trans meso* acid esterified two hundred times faster than the *cis meso* acid. The rate variation in the hydrolysis was only five-fold and in the reaction of phenacyl bromide with the sodium salts, the *cis meso* compound reacted about twice as fast as the other two. The *meso trans* isomer reacted at about the same rate as trimethylacetic acid or ester in the esterification and hydrolysis, but all isomers reacted more slowly than diisopropylacetic acid or ester, the most nearly similar aliphatic compound.

LOS ANGELES, CALIFORNIA RECEIVED SEPTEMBER 17, 1949

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE OHIO STATE UNIVERSITY]

The Synthesis of Polynuclear Aromatic Hydrocarbons. I. Methyl-1,2-benzanthracenes[1]

BY MELVIN S. NEWMAN[*] AND RUSSELL GAERTNER[†]

Although many polynuclear aromatic hydrocarbons and their derivatives have been prepared and evaluated as to physiological action, there has not yet emerged a true correlation of carcinogenic activity with any other known property of these molecules. This has been due in part to the fact that investigators have not had sufficient access to whole series of compounds and have had to conduct their experiments with relatively few members. Accordingly we have undertaken to make all twelve of the monomethyl-1,2-benzanthracenes and the six monomethylbenzo[c]phenanthrenes in large enough amounts so that research workers may initiate experiments with the assurance that all of these compounds will soon be available. It is hoped that all members of each series will be tested for carcinogenic activity by several methods so that a more significant evaluation of the carcinogenic potency can be made than is possible at present.[2]

This communication describes the methods used to prepare appreciable quantities of 1,2-benzanthracene, of 9,10-dimethyl-1,2-benzanthracene and of 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 2′- and 3′-methyl-1,2-benzanthracenes. Since our main objective was the preparation of sufficient quantities of these materials for biological evaluation, we do not claim to have found the best methods for preparing each of the compounds herein listed. However, several improvements over literature syntheses have been made and recorded. All of these hydrocarbons had been prepared previous to the start of this work. The melting points of all of the monomethyl-1,2-benzanthracenes have been listed.[3] Since that publication the following additional syntheses (through 1948) have been reported: 3-methyl-,[4] 4-methyl-,[5a,b] 5-methyl-,[6a,b] 6-methyl-,[7] 8-methyl-,[8a,b] 9-methyl-,[9a,b] 10-methyl-,[10a,b,c,d,e,f] 1′-methyl-,[11] 2′-methyl-,[12] 4′-methyl.[13] The only significant change in properties over those listed previously[3] is in the case of 8-methyl-1,2-benzanthracene which has a melting point of 118.0–118.5°[8a,b] instead of 107°.[3]

The syntheses of 1,2-benzanthracene according to Badger and Cook[14] and of 10-methyl-1,2-benz-

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(1) The work herein reported was supported by a grant, C-483, from the U. S. Public Health Service to whom grateful acknowledgment is made. This grant included funds for a postdoctorate fellowship to Dr. Russell Gaertner and part time research assistantships to Philip Beal, III, and Milton Wolf. We are indebted to these men for the preparation of many research intermediates.

(2) The compounds herein described are being evaluated by Dr. I. Berenblum at the National Cancer Institute, Bethesda, Md.

(3) J. W. Cook and A. M. Robinson, *J. Chem. Soc.*, 505 (1938).

(4) M. S. Newman and R. T. Hart, THIS JOURNAL, **69**, 298 (1947).

(5) (a) L. F. Fieser and R. N. Jones, *ibid.*, **60**, 1942 (1938); (b) W. E. Bachmann, M. W. Cronyn and W. S. Struve, *J. Org. Chem.*, **12**, 596 (1947).

(6) (a) W. E. Bachmann and A. L. Wilds, THIS JOURNAL, **60**, 624 (1938); (b) W. E. Bachmann, *J. Org. Chem.*, **3**, 434 (1938).

(7) W. E. Bachmann and J. M. Chemerda, *ibid.*, **6**, 36 (1941).

(8) (a) L. F. Fieser and Wm. S. Johnson, THIS JOURNAL, **61**, 168, 1647 (1939); (b) (Mrs.) J. W. Cook, A. M. Robinson and E. M. F. Roe, *J. Chem. Soc.*, 266 (1939).

(9) (a) L. F. Fieser and E. B. Hershberg, THIS JOURNAL, **62**, 49 (1940); (b) C. K. Bradsher, *ibid.*, **62**, 1077 (1940).

(10) (a) L. F. Fieser and J. L. Hartwell, *ibid.*, **60**, 2555 (1938); (b) L. F. Fieser and E. B. Hershberg, *ibid.*, **61**, 1272 (1939); (c) A. Dansi and C. Ferri, *Gazz. chim. ital.*, **69**, 195 (1939); (d) J. L. Wood and L. F. Fieser, THIS JOURNAL, **62**, 2674 (1940); (e) B. M. Mikhailow, *Izvest. Akad. Nauk S. S. S. R., Otdel Khim. Nauk*, 619 (1946); *C. A.*, **42**, 6351d (1948); (f) B. M. Mikhailow and T. K. Kozminskaya, *Doklady Akad. Nauk S. S. S. R.*, **59**, 509 (1948); *C. A.*, **42**, 6792e (1948).

(11) W. E. Bachmann and R. O. Edgerton, THIS JOURNAL, **62**, 2550 (1940).

(12) W. E. Bachmann and G. D. Cortes, *ibid.*, **65**, 1329 (1943).

(13) A. Sempronj, *Gazz. chim. ital.*, **70**, 615 (1940).

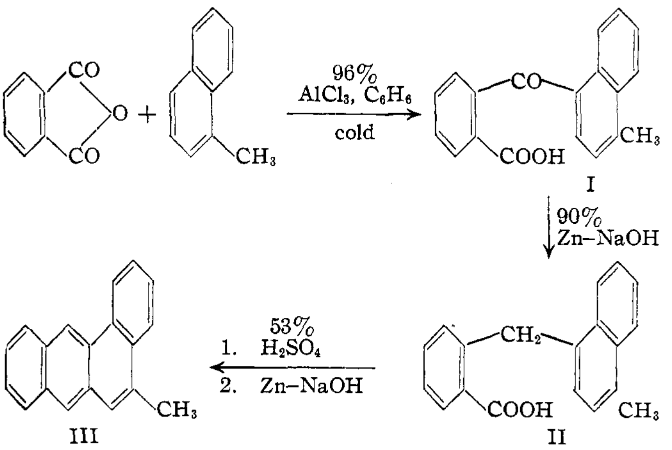
(14) G. M. Badger and J. W. Cook, *J. Chem. Soc.*, 802 (1939).

anthracene according to Wood and Fieser[10d] proceeded satisfactorily without modification. The other compounds were prepared either by modification of published methods or by new methods.

The conversion of *o*-benzoylnaphthoic type acids into benzanthracenes has been effected by several methods. In the present cases, the most effective conversions involved the following steps: reduction of a benzoylnaphthoic type acid to a lactone by boiling with hydriodic acid in a phosphoric–acetic acid mixture, saponification of the lactone with aqueous alcoholic alkali followed by reduction to a benzylnaphthoic type acid by boiling with zinc dust and alkali, ring closure with sulfuric acid to a benzanthrone, and reduction to a benzanthracene by boiling with zinc dust and alkali. On the other hand, naphthoylbenzoic acids were reduced directly to the corresponding naphthylmethylbenzoic acids by boiling with alkali and zinc dust.

In discussing the remaining syntheses herein described the compounds are grouped according to the general synthetic scheme involved. Unless otherwise stated, yields and properties of previously reported compounds were in substantial agreement with those mentioned in the original papers.

3-Methyl-1,2-benzanthrene.—Our synthesis of this compound was modelled after previous syntheses[15,16] and is shown in the chart.



To a stirred cooled mixture of 111 g. (0.75 mole) of phthalic anhydride and 107 g. (0.75 mole) of 1-methylnaphthalene[17] in 1 kg. of pure sulfur-free benzene was added in portions during forty-five minutes 210 g. (1.6 moles) of aluminum chloride, the internal temperature being kept below 10°. About fifteen minutes after the addition had been completed, a solid began to separate and the evolution of hydrogen chloride became copious. After stirring for another ninety minutes in the cold, the mixture was poured on ice and hydrochloric acid. The crude keto-acid was crystallized from benzene to yield 216 g. (90% as the crystals contained about 9% of benzene of crystallization) of 2-(4-methyl-1-naphthoyl)-benzoic acid (I).

A mixture of 25 g. of this solvated acid, 30 g. of activated zinc dust (copper couple) and 400 ml. of 10% sodium hydroxide was refluxed for forty hours. The product was recrystallized from benzene to yield 19.8 g. (90%) of colorless fine needles, m. p. 185–187°,[18] of 2-(4-methyl-1-naphthylmethyl)-benzoic acid (II). The best yield of III was obtained in an experiment in which 70 g. of crude II was dissolved with stirring in 700 ml. of concentrated sulfuric acid and allowed to stand for ninety minutes. This solution was poured on ice and the crude benzanthrone was refluxed with a mixture of 150 g. of activated zinc dust and 1850 ml. of 10% sodium hydroxide for eleven hours to yield 28.5 g. (53%) of light yellow plates, m. p. 151.5–154.0°, of III. The 3-methyl-1,2-benzanthracene was purified further by recrystallization of the picrate and by chromatography over alumina to yield colorless platelets, m. p. 155.9–156.9°.[19]

4-Methyl-1,2-benzanthracene.—Our synthesis of this hydrocarbon was modelled after that of Fieser and Jones[5a] and involves several improvements. The steps are shown in the chart (p. 266).

The main improvement lies in the use of pure methyltetralin obtained by reduction of 7-methyl-1-tetralone instead of the mixture of methyltetralins obtained on hydrogenation of 2-methylnaphthalene.[5a,20]

To a stirred solution of 20 g. of pure 6-methyl-1,2,3,4-tetrahydronaphthalene[21] and 21.7 g. of phthalic anhydride in 80 ml. of pure benzene maintained at about 65° was added 40 g. of anhydrous aluminum chloride during thirty minutes. After stirring at 65° for six hours the red viscous mixture was poured on ice and hydrochloric acid. The keto-acid was crystallized from a benzene–petroleum ether mixture to yield 34.8 g. (87%) of colorless slightly impure keto-acid, IV, m. p. 161–165°, lit.[5a] m. p. 167.5–168.0° for pure acid. This material was satisfactory for the next step in which the keto-acid, IV (120 g.), was reduced to V, m. p. 167–169°, in 84% yield.

The conversion of V to VI was best carried out without attempting to isolate the tetrahydrobenzanthracene intermediate. The acid V (104 g.) was cyclized as usual with sulfuric acid (8 ml. per g.) and the crude anthrone reduced by refluxing with activated zinc and sodium hydroxide solution using a toluene layer. After removal of volatile solvents, the residue (99 g.) was heated at about 335° for two hours and at 350° for forty-five minutes over 5 g. of a 10% palladium-on-charcoal catalyst.[22] By addition of alcohol to a filtered benzene extract of the reaction mixture there was obtained 63.6 g. (69%) of pale yellow needles of VI, m. p. 122.5–124°. A pure colorless sample, m. p. 126.2–127.2°,[19] was obtained by chromatography over alumina.

Attempts to cyclize IV to a benzanthraquinone with 25% fuming sulfuric acid[20] at 60–70°, with benzoyl chloride–sulfuric acid,[14] and with phthalic anhydride–sulfuric acid[23]

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(15) J. W. Cook, *J. Chem. Soc.*, 1087 (1930).

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

(17) Pure α-methylnaphthalene was prepared from α-tetralol (courtesy of the Koppers Co., Pittsburgh, Pa.) by oxidation to α-tetralone, reaction with methylmagnesium bromide (according to L. I. Smith and Chien-Pen Lo, THIS JOURNAL, **70**, 2209 (1948)), dehydration of the carbinol, and dehydrogenation (in 80% yield) by heating with an equivalent of sulfur at 230° for six hours.

(18) All melting points corrected unless otherwise noted.

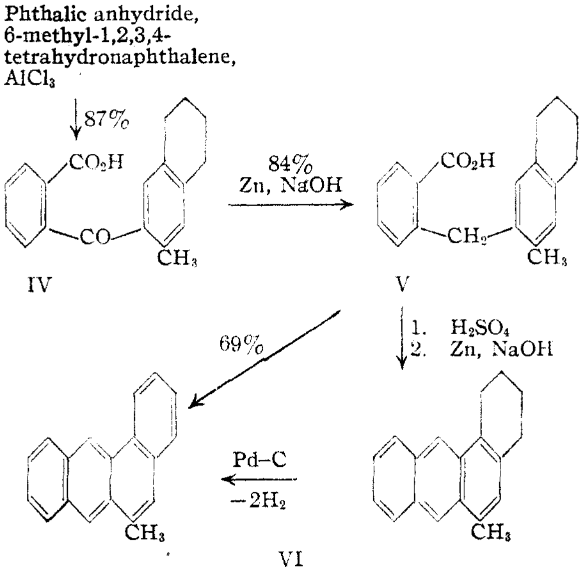
(19) These melting points represent higher values than are recorded in the literature.

(20) G. Schroeter, *Ber.*, **54**, 2242 (1921).

(21) The 6-methyl-1,2,3,4-tetrahydronaphthalene, b. p. 61–62° at 1 mm., n^{25}_{D} 1.5315, was prepared in 84% yield (compare Krollpfeiffer and Schafer, *ibid.*, **56**, 620 (1923)) by a Clemmensen–Martin reduction.

(22) N. D. Zelinsky and M. B. Turowa-Pollak, *ibid.*, **58**, 1292 (1925).

(23) H. Waldmann, *J. prakt. Chem.*, **150**, 121 (1938).



failed. The Clemmensen-Martin reduction of IV gave only a fair yield of impure V, while IV was recovered unchanged from an attempted reduction to the corresponding lactone by the hydriodic-phosphoric acid reduction used successfully for reduction of benzoylnaphthoic acid types.

One unsuccessful attempt was made to reduce the keto-group of IV with the hydrogens of the tetrahydro ring by heating the methyl ester of the keto-acid, IV, with palladium-on-charcoal[24] at 330°. However, 60% of impure starting material was obtained.

5-Methyl- and 7-Methyl-1,2-benzanthracene.—Since the synthesis of 5-methyl-1,2-benzanthracene by Fieser and Newman[25] appeared to be applicable to the preparation of the 5-, 6- and 7-methyl isomers, we chose this method. The chief development here was the improvement of the conversion of the benzoylnaphthoic type acids to benzylnaphthoic type acids by a two step reduction process: the first step involved reduction to a lactone by hydriodic and phosphoric acids; the second step, an hydrolysis to a hydroxy-acid salt followed by reduction by boiling with zinc dust and alkali. The three isomers were made by this general procedure; however, the 6-isomer, Xb, was obtained in a pure condition only from XIII. The attempted synthesis of Xb by the general procedure from IXb yielded a mixture of hydrocarbons, undoubtedly 6- and 8-methyl-1,2-benzanthracenes, formed by ring closure ortho and para to the methyl group. This is quite unusual since such closures usually involve only the position para to the methyl group. The best method for the synthesis of Xb is described later.

Some improvement (on large runs) in the yield of keto acids, VII, was noticed if the diarylcadmium derivatives were used in place of the Grignard reagents. The reactions involved are outlined in the chart.

5-Methyl-1,2-benzanthracene.—2-(*o*-Toluyl)-1-naphthoic acid (VII) was prepared in 46% yield from *o*-tolylmagnesium bromide and 1,2-naphthoic anhydride[26] as before.[25] An attempted reaction of the anhydride by the low temperature method of Newman and Smith[27] resulted in a 73% recovery of the anhydride. Reduction of VII to the lactone, VIII, m. p. 158–159°, previously obtained in low yield as a reduction product after an attempted Grignard reaction,[25] was accomplished in 82% yield by refluxing (typically) a mixture of 5 g. of VII, 1 g. of potassium iodide, 3 g. of red phosphorus, 30 ml. of 85% phosphoric acid, 30 ml. of acetic acid and 5 ml. of water for six hours. This lactone was reduced to IX in 88% yield by following a procedure previously described for a similar lactone.[28] The first acid, IX, obtained melted at 143.5–144.5°, in agreement with the earlier work,[28] but later samples melted at 151–152°. A mixture of the two forms melted at 151–152°.

Anal. Calcd. for $C_{19}H_{16}O_2$: C, 82.6; H, 5.8. Found[29c]: C, 82.7, 82.4; H, 6.0, 5.9.

The remaining steps followed previous procedures.[25] A colorless sample of X, obtained from recrystallized picrate, melted at 160.0–160.6°.[19]

A number of methods of ring closure and of reduction were investigated with the keto-acid, VII. Treatment with benzoyl chloride and sulfuric acid at 130°, a method previously used for the conversion of *o*-(1-naphthoyl)-benzoic acid to benzanthraquinone, produced small amounts of an impure quinone, isolated by vatting. Similar results were obtained using fused zinc chloride as the catalyst, but fusion with zinc chloride at 180° gave a dark material which did not reduce in the vat test. Heating with phosphorus pentoxide in nitrobenzene[30] at 160–165° gave only a black, insoluble resin.

Reduction of VII with Raney nickel-aluminum alloy and sodium hydroxide[31] yielded only a very small amount of impure lactone and a gummy acid fraction. Hydrogenation over copper chromite[32] resulted in the recovery (25%) of the keto-acid, and produced non-crystalline acids and neutral material. The Clemmensen reduction, either by the Martin modification or in acetic acid, was unsuccessful. Treatment with isopropylmagnesium bromide or 3% sodium amalgam gave only very small amounts of the lactone, along with gummy acids and starting material. When the acid was esterified with dodecyl mercaptan by azeotropic distillation with benzene and the excess mercaptan removed by distillation at reduced pressure, the viscous oil which remained (probably a pseudo thio-ester) gave a low yield of impure lactone when refluxed in ethanol with Raney nickel catalyst[33] cured at 50°.

The keto-acid was also subjected to reduction with lithium aluminum hydride in the usual way. From 5 g. of VII were obtained 2.7 g. of lactone, m. p. 157–159°, and (after separation by alkaline saponification) 0.75 g. of another neutral substance, m. p. 158.5–160° after recrystallization from ethanol. This compound, presumably (1-hydroxymethyl-2-naphthyl)-*o*-tolylcarbinol, depressed the melting point when mixed with the lactone. It formed hard white crystals from ethanol; m. p. 159.8–161°.

Anal. Calcd. for $C_{19}H_{18}O_2$: C, 82.0; H, 6.5. Found^c: C, 82.4, 82.3; H, 6.8, 6.7.

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[24] M. S. Newman and H. V. Zahm, This Journal, **65**, 1097 (1943); M. S. Newman and T. J. O'Leary, *ibid.*, **68**, 258 (1946).

[25] L. F. Fieser and M. S. Newman, *ibid.*, **58**, 2376 (1937).

[26] E. B. Hershberg and L. F. Fieser, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1947, pp. 194, 423.

[27] M. S. Newman and A. S. Smith, *J. Org. Chem.*, **13**, 592 (1948).

[28] M. S. Newman, This Journal, **60**, 1369 (1938).

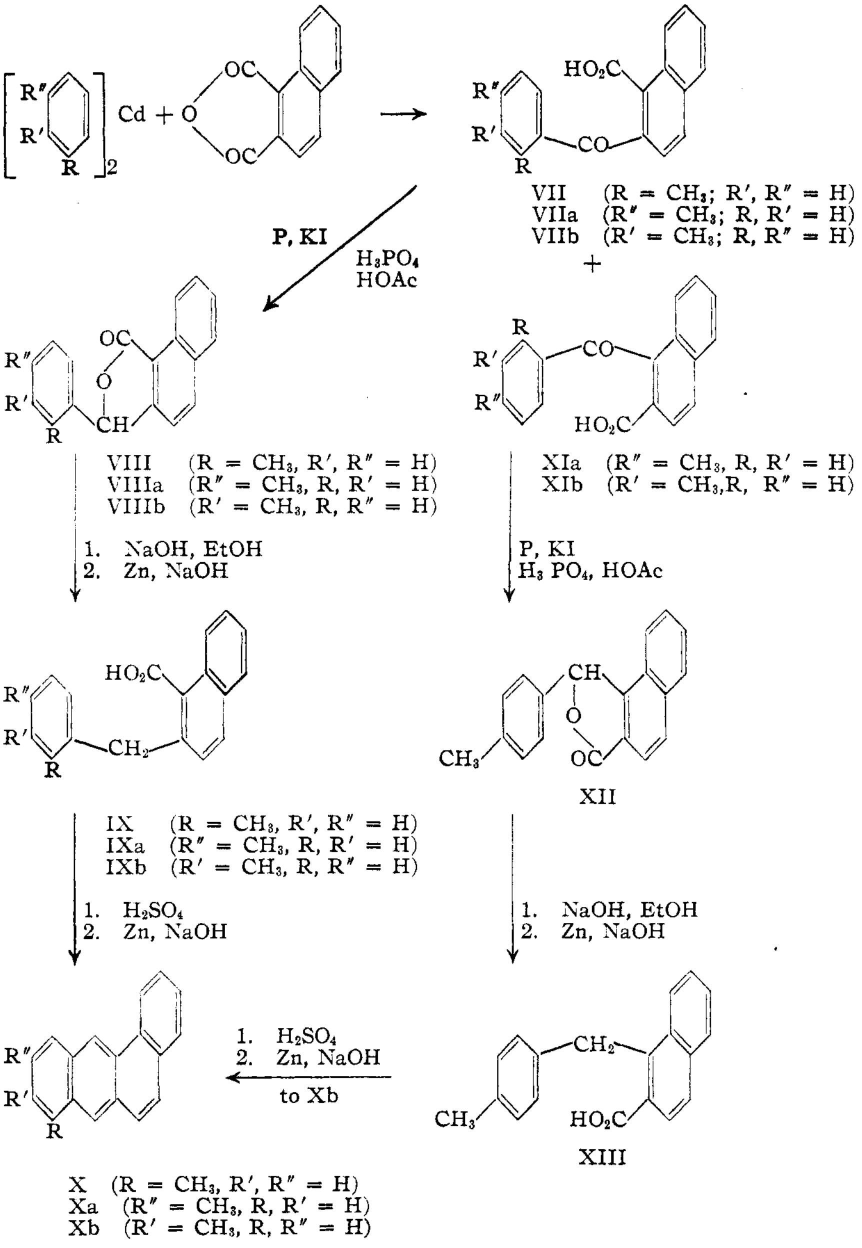
[29] Analyses marked with a ^{c} were carried out by the Clark Microanalytical Laboratory, Urbana, Ill.; those marked with a ^{k} by Mrs. Edith Klotz at The Ohio State University.

[30] R. Sandin and L. F. Fieser, This Journal, **62**, 3098 (1940).

[31] D. Papa, E. Schwenk and B. Whitman, *J. Org. Chem.*, **7**, 587 (1942).

[32] L. F. Fieser and E. B. Hershberg, This Journal, **59**, 1028 (1937).

[33] R. Mozingo, D. E. Wolf, S. A. Harris and K. Folkers, *ibid.*, **65**, 1013 (1943).



When this compound was treated with sulfuric acid at room temperature, the solution turned red, then green, but no hydrocarbon or starting material could be isolated from the hydrolyzed mixture.

7-Methyl-1,2-benzanthracene.—The synthesis was similar to the improved synthesis of 5-methyl-1,2-benzanthracene already described. In the best run, an organocadmium compound[34] was prepared from the Grignard reagent from 275 g. of *p*-bromotoluene (1.6 moles) and 39 g. of magnesium turnings in 1 l. of ether and 400 ml. of benzene. To the reagent was added 146 g. (0.8 mole) of anhydrous cadmium chloride and the mixture was refluxed for ninety minutes to complete the reaction. Then 152 g. (0.75 mole) of 1,2-naphthalic anhydride was added to the warm mixture over twenty minutes and the refluxing continued two hours. A dark viscous layer separated and soon solidified, allowing stirring only in the supernatant solvent layer. Decomposition with dilute hydrochloric acid was quite slow even with external heating but eventually all the dark solid dissolved to form a light yellow solution. The acids were isolated by carbonate extraction and crystallized from the minimum amount of benzene, allowing a day or so for complete separation.

Separation of the isomers was accomplished preferably by recrystallization of this product from benzene, the first flocculent solid being removed by filtration within an hour or so. This was rather pure lower-melting isomer, m. p. 183–184°. A total of 75 g. (34.5% yield) of this material was obtained by suitable concentration of the mother liquors. A sample was recrystallized from benzene giving white flakes, m. p. 183–184°. Subsequent transformations showed it to be 2-(*p*-toluyl)-1-naphthoic acid, VIIa.

Anal. Calcd. for C$_{19}$H$_{14}$O$_3$: C, 78.6; H, 4.9. Found[c]: C, 78.5, 78.3; H, 5.0, 5.2.

When the mother liquors from the above recrystallization were allowed to stand for some time before concentration, dense white crystals of a higher-melting isomer separated. By suitable repeated treatment, a total of 23.9 g. (11% yield) was obtained, m. p. 223–226°. A pure sample of XIb recrystallized from benzene melted at 226–227°.

Anal. Calcd. for C$_{19}$H$_{14}$O$_3$: C, 78.6; H, 4.9. Found[c]: C, 78.3, 78.5; H, 5.1, 5.2.

The same isomers were obtained by a Grignard procedure similar to that described[25] for the *o*-tolyl isomers. The best yields on a small scale (20 g. of anhydride) were 23% of VIIa and 3.6% of XIa. Using 200 g. of the anhydride, the yields were 17.3 and 4.5%. Separation of the isomers was also accomplished by stepwise acidification of a solution of the potassium salts, followed by recrystallization; this involved more manipulation with no better results, although it was more reliable, the non-equilibrium crystallization technique occasionally giving erratic results, necessitating a larger number of operations.

A fair amount (11 g.) of 6-methyl-1,2-benzanthracene, Xb, was made from XIa by a similar general procedure. The keto-acid XIa (45 g.) yielded 44 g. of crude lactone, XII, m. p. 150–160°. A pure sample recrystallized for analysis from benzene formed hard colorless crystals, m. p. 167.0–168.2°.

Anal. Calcd. for C$_{19}$H$_{14}$O$_2$: C, 83.2; H, 5.2. Found[c]: C, 83.1, 83.1; H, 5.2, 5.0.

Reduction of impure lactone (42.5 g.) gave 27 g. of crude 1-(*p*-methylbenzyl)-2-naphthoic acid (XIII) m. p. 171–182°. A pure sample, recrystallized from benzene, melted at 192.4–193.0°.

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[34] The reaction of arylcadmium compounds with anhydrides has been described by de Benneville, *J. Org. Chem.*, **6**, 423 (1941).

Anal. Calcd. for $C_{19}H_{16}O_2$: C, 82.6; H, 5.8. Found[c]: C, 82.3, 82.5; H, 5.8, 5.8.

Upon the usual sulfuric acid cyclization and zinc–sodium hydroxide reduction, 24 g. of crude acid, XIII, yielded 11.1 g. of almost colorless Xb, m. p. 146–148°. The over-all yield, based on XIa, was 34%. A sample purified by further recrystallization from benzene–alcohol melted at 151.5–152.5°.[19]

Reaction of the lithium salt of 1,2-naphthalic acid with *p*-tolyllithium was investigated.[35] The lithium salt was prepared in 85% yield by dissolving the anhydride in a hot concentrated solution of lithium hydroxide, cooling in ice, and oven-drying the precipitate. Only 1,2-naphthalic acid was isolated from the reaction with *p*-tolyllithium.

Reduction of VIIa was best accomplished by the phosphorus–hydriodic acid procedure. In the best run, 43 g. of the keto-acid yielded 25.3 g. (63%) of lactone, m. p. 305–312° dec., recrystallized from benzene–petroleum ether, b. p. 60–70° (Skellysolve B). A sample for analysis formed colorless crystals, m. p. 316–318° dec. Since the molecular weight (ebullioscopic, benzene) was 464 (calcd. for dimer, 552) this lactone is probably dimeric. A similarly high melting dimeric lactone was obtained in the case of the corresponding meta derivative.

Anal. Calcd. for $C_{19}H_{14}O_2$: C, 83.2; H, 5.2. Found[c]: C, 83.3, 83.5; H, 5.0, 5.0.

Reduction of the above lactone (24.3 g.) by the zinc–sodium hydroxide procedure gave 21.6 g. (86%) of 2-(*p*-tolyl)-1-naphthoic acid (IXa) m. p. 161–164°. Recrystallization from benzene–Skellysolve B raised the melting point to 168.2–169.2°.

Anal. Calcd. for $C_{19}H_{16}O_2$: C, 82.6; H, 5.8. Found[k]: C, 82.8, 82.8; H, 6.4, 6.3.

Conversion of IXa to 7-methyl-1,2-benzanthracene (Xa) was highest on a small run. By the usual method, 0.55 g. of IXa gave 0.27 g. (56%) of Xa which separated from ethanol–benzene in pure light yellow plates. The highest melting point was 183.0–183.6.[19] When the synthesis was carried through without purification of intermediates the best over-all yield of hydrocarbon from keto-acid was 24%.

Unsuccessful experiments included an attempted closure of the keto-acid with phosphoric acid containing phosphorus pentoxide ("Tetraphosphoric Acid," Monsanto Chemical Co.) at 140°, which gave only a small amount of colored high-melting neutral material.

Application of the modified Wolff–Kishner reduction[36] to VIIa gave an equal weight of quite insoluble nitrogen-containing compound melting at 267–270°. Analysis of a colorless sample, m. p. 276.4–277.4°, recrystallized from toluene, gave values consistent with a formulation as 1-hydroxy-4-*p*-tolyl-2,3-diazaphenanthrene.

Anal. Calcd. for $C_{19}H_{14}ON_2$: C, 79.7; H, 4.9; N, 9.8. Found[c]: C, 80.5, 80.3; H, 5.0, 4.9; N, 9.4, 9.5.

Electrolytic reduction of VIIa in ethanol and sulfuric acid gave resinous material, and a Clemmensen reduction also failed.

The reaction of 1,2-naphthalic anhydride with *m*-tolylmagnesium bromide was not investigated; the procedure with the cadmium derivative was similar to that described above for the para isomer, including separation procedures. From 20 g. of anhydride were obtained 2-(*m*-toluyl)-1-naphthoic acid (VIIb) (7.33 g., 25.3%), m. p. 179–183° and 1-(*m*-toluyl)-2-naphthoic acid (XIb) (1.5 g., 5.2%); m. p. 218–220°. Recrystallization of the low-melting acid from ethanol–benzene gave flocculent white plates, m. p. 185.4–187.4°. The high-melting isomer separated from benzene in compact white crystals, m. p. 220.3–221.1°.

Anal. Calcd. for $C_{19}H_{14}O_3$: C, 78.6; H, 4.9. Found[k]: (187° isomer) C, 78.8, 78.6; H, 5.0, 4.9; (221° isomer) C, 78.6, 78.8; H, 4.8, 4.7.

In the single large-scale run attempted (272 g. of anhydride, 35 g. recovered), the yields dropped unaccountably to 10.5 and 3%, respectively.

The lower-melting isomer was subjected to the same treatment described in the synthesis of 7-methyl-1,2-benzanthracene. Reduction to the lactone, although accomplished in the usual way, was unusual in that two compounds were isolated. From 5.0 g. of the acid were obtained 2.25 g. of lactones, of which about 0.3 g. was a high-melting compound. It could be separated by dissolving the whole in benzene, concentrating to about 5 ml., adding Skellysolve B until a hard compact crust separated. Recrystallization in the same way gave colorless crystals, m. p. 324–325° dec. The structure of this compound is unknown, but we believe it may be a dimeric lactone formed after pinacolic reduction of the keto group of VIIb. This formulation is supported by analysis, by molecular weight determinations (ebullioscopic in benzene) and the high melting point. On further reduction, however, this high melting compound yielded the same acid, IXb, as was obtained from the low melting lactone, VIIIb.

Anal. Calcd. for $C_{38}H_{26}O_4$: C, 83.8; H, 4.8. Found[k]: C, 83.8, 83.3; H, 4.7, 4.9.

The low-melting isomer was obtained from the solution from which the above compound separated. Recrystallization from benzene gave white needles of the lactone of 2-(α-hydroxy-*m*-methylbenzyl)-1-naphthoic acid (VIIIb) m. p. 147.6–148.2°.

Anal. Calcd. for $C_{19}H_{14}O_2$: C, 83.2; H, 5.2. Found[k]: C, 83.4, 83.0; H, 5.0, 5.3.

Both of the above compounds gave the same compound, 2-(*m*-methylbenzyl)-1-naphthoic acid (IXb) on reduction with zinc–sodium hydroxide. The yield from the low-melting compound was quantitative on a small scale; recrystallized from benzene–Skellysolve B, the white crystals melted at 127.2–128.2°.

Anal. Calcd. for $C_{19}H_{16}O_2$: C, 82.6; H, 5.8. Found[k]: C, 82.8, 82.8; H, 5.7, 5.5.

From 0.75 g. of this acid was obtained 0.32 g. (48%) of apparently heterogeneous hydrocarbon by the usual closure and reduction. From ethanol–benzene the powder melted at 135–140°. When the synthesis was carried through without isolation of intermediates, 37 g. of keto acid (low-melting isomer) yielded 7.4 g. (24%) of the hydrocarbon mixture, presumably composed of 6- and 8-methyl-1,2-benzanthracenes. Attempted separation by chromatography, using Skellysolve C as the solvent and eluting with a mixture containing increasing amounts of benzene, failed to effect any appreciable separation.

3′-Methyl-, 6-Methyl- and 8-Methyl-1,2-benzanthracene.—These hydrocarbons have been prepared by the method recently developed for the synthesis of 1,2-benzanthracene.[4] The reduction of the diketone, XVII, by lithium aluminum hydride and other slight modifications was found advantageous. The structures of the keto acids, XX, are assumed as shown because this structure was established in the unmethylated analog.[4] However, in one case, the isolation of 3 isomeric keto-acids proves that at least one of these must have had the alternate structure, 3-carboxy-4-benzyl-7-methyl-1-keto-1,2,3,4-tetrahydronaphthalene. The reactions are outlined in the chart.

3′-Methyl-1,2-benzanthracene.—The required benzyl *p*-tolyl ketone,[37] m. p. 108–110°, was prepared in 79% yield (recrystallized) from 232 g. of phenylacetyl chloride, 1200 ml. of pure toluene and 226 g. of anhydrous aluminum chloride by stirring at room temperature for one hour.

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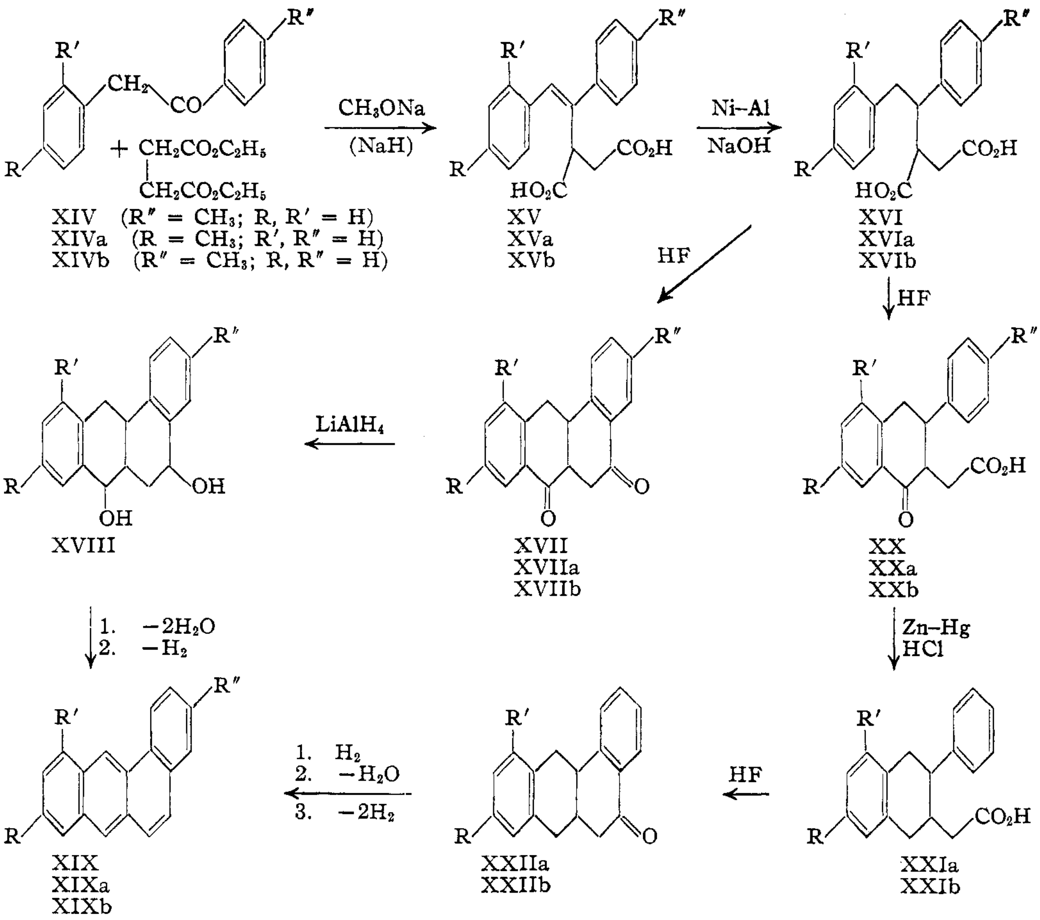
[35] Modeled after the general procedure of van Dorp and Arens, *Rec. trav. chim.*, **65**, 338 (1946).

[36] Huang-Minlon, THIS JOURNAL, **68**, 2487 (1946).

[37] H. Strassman, *Ber.*, **22**, 1229 (1889).



The use of sodium hydride,[38] potassium *t*-butoxide,[39] and sodium methoxide[4] as condensation agents in the Stobbe reaction were studied. Heating was necessary in all cases, benzene being used as a solvent with sodium hydride. The highest yield of crystalline dicarboxylic acid XV (63%) resulted from the use of potassium *t*-butoxide, only 13% of this material being isolable from the sodium hydride reaction. However, it proved expedient to hydrolyze and reduce the solution of the salt without attempting isolation of the unsaturated diacid. On the basis of a run which yielded 82% of saturated diacids from the crystalline ethylenic acids, the Stobbe condensation using either sodium hydride or sodium methylate proceeded in 64% yield. In the larger runs, the latter was used because of its general convenience.

The best yield of crystalline XV was obtained when a solution of 2.2 g. of potassium in 50 ml. of *t*-butyl alcohol was added to a solution of 10.5 g. of XIV in 13.1 g. of diethyl succinate. After heating to reflux for one hour the mixture was treated with dilute hydrochloric acid. When difficulty was met in trying to crystallize the half-ester, it was saponified with 20% ethanolic sodium hydroxide. The diacid (9.65 g., 64%) was obtained by crystallization from benzene.

The crude crystalline unsaturated acid, XV, from any source melted at 90–95°. Recrystallization from benzene gave colorless crystals, m. p. 94–97°, which was probably a mixture of isomers and required long drying at 80° under reduced pressure to remove the last trace of solvent.

Anal. Calcd. for $C_{19}H_{18}O_4$: C, 73.5; H, 5.9. Found[k]: C, 73.7, 73.7; H, 5.7, 5.8.

Reduction[4] of 15 g. of the above crude XV yielded 7.55 g. of material, m. p. 198–200°, which precipitated during concentration of the ether–benzene extracts, and 4.75 g., m. p. 144–147°, which separated only from a cold, concentrated benzene solution. The total yield was 82%.

The high-melting isomer, XVI, separated from benzene–ethanol in colorless crystals, m. p. 205–206° dec. The lower-melting XVI formed colorless crystals from benzene, m. p. 148.6–150.6°.

Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.1; H, 6.5. Found[k]: (206° isomer), C, 73.1, 73.0; H, 6.0, 6.1; (150° isomer), C, 73.2, 73.1; H, 6.2, 6.4.

In the best large run, without isolation of the intermediate unsaturated diacid, 52.5 g. of benzyl *p*-tolyl ketone gave 25.9 g. and 15.6 g. (total over-all yield, 53%), respectively, of the high- and low-melting forms of XVI. The best yield was obtained when the sodium methylate was added to the equimolar mixture of ketone and ester at 60–70°; at this temperature no immediate temperature effect was noted, but when the reagent was added at 80–90° the reaction became violent and the yield was lower. Heating was then continued to a bath temperature of 130–140° for an hour. Water (200 ml.) and an equal volume of 20% sodium hydroxide were added and heating continued for six hours. The cooled mixture was extracted with ether–benzene and the dark aqueous layer diluted to 1 l. Eighty grams of sodium hydroxide and then, with stirring at 90°, 120 g. of nickel–aluminum alloy were added during six hours (octyl alcohol controlled foaming). Acidification of the filtrates in the presence of ether–benzene yielded the colorless saturated acids, XVI.

Double ring closure of these compounds was best accomplished with anhydrous hydrogen fluoride.[4] A mixture of the acids, 43.6 g., was stirred mechanically into

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[38] G. H. Daub and W. S. Johnson, THIS JOURNAL, **70**, 418 (1948).

[39] W. S. Johnson and A. R. Jones, *ibid.*, **69**, 792 (1947).

about 500 ml. of the cold condensing agent which was allowed to evaporate overnight. The residue was heated at 40–50° for another day, benzene added, and the whole poured into excess sodium carbonate solution, 18.2 g. of high-melting diketone, XVII, m. p. 230–235°, being obtained. In some runs a troublesome red-orange color developed; however, the colored diketones were suitable for reduction. A total of 7.4 g. of impure lower-melting compound, m. p. 155–180°, was obtained from the solvent layer. The total yield of diketones, XVII, was 66%.

The high-melting diketone, XVII, was recrystallized from benzene, in which it was quite difficultly soluble, giving colorless crystals, m. p. 233.5–235.5° decomp. For preliminary purification, tetrachloroethane was a better solvent. Recrystallized from benzene, the lower-melting diketone, XVII, formed colorless needles, m. p. 181.5–182.5° dec.

Anal. Calcd. for $C_{19}H_{16}O_2$: C, 82.6; H, 5.8. Found[k]: (235° isomer) C, 82.3, 82.8; H, 5.8, 5.6; (182° isomer[c]) C, 82.6, 82.4; H, 5.7, 5.6.

From the aqueous layer, 3.7 g. of a mixture of keto-acids was obtained; m. p. 135–160°. From several runs, by recrystallization from benzene and manual separation of the various types of crystals, three different (not isomorphic forms) keto-acids, XX, were isolated. All were obtained as colorless crystals from benzene and melted at 142–143°, 200.0–200.6° and 215–217°.

Anal. Calcd. for $C_{19}H_{18}O_3$: C, 77.5; H, 6.2. Found[c]: (143° isomer) C, 77.2, 77.3; H, 6.1, 5.9, (200° isomer) C, 77.5, 77.2; H, 5.9, 5.7; (217° isomer) C, 77.6, 77.7; H, 6.1, 6.1.

Attempted closure of chlorides of the diacids with aluminum chloride or stannic chloride was much inferior to the above procedure. When the keto-acid mixture mentioned above (14.5 g.) was again dissolved in 200 ml. of hydrogen fluoride only 4.9 g. of diketones was obtained. Closure of the 6.25 g. of recovered acids from this run by the phosphorus pentachloride–aluminum chloride method gave largely resinous neutral products and some unchanged acids. Even in the hydrogen fluoride method, a considerable amount of material could not be accounted for, even as tar, of which only a small amount was obtained.

Although the Meerwein–Ponndorf–Verley method and subsequent heating with palladium–charcoal was investigated for the conversion of the diketones to the hydrocarbon (yield 35%), reduction with lithium aluminum hydride was much superior. The ether-insoluble diketone, XVII, was added as a powder to a 25–50% excess of the reagent in ether; an exothermic reaction ensued instantaneously. Stirring was continued at room temperature for an hour. Acidification of the mixture, followed by separation of the insoluble product by filtration, washing thoroughly with ammonia, and oven-drying, gave the crude diol, XVIII. The yield from pure high-melting diketone was quantitative. The compound was almost insoluble in the usual solvents and could be purified only with difficulty. It was recrystallized for analysis from *n*-butanol, from which it separated as a mass of fine needles, m. p. 240–241.5°.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.4; H, 7.2. Found[c]: C, 81.5, 81.4; H, 7.3, 7.3.

In most runs, this solid was placed in a two-bulb distilling flask with the dark-colored oils remaining after the removal of the solvents in the organic layer of the filtrate. The mixture was heated to about 200° and a crystal of iodine added from time to time. When dehydration appeared complete (thirty minutes), the residue was cooled and the theoretical amount of sulfur added. Heating was resumed for an hour at 230–250°, the neck of the flask sealed off, and the residue distilled *in vacuo*. The distillate, a light yellow oil which solidified, was dissolved in benzene, chromatographed on alumina (removing a colored and otherwise persistent impurity), and crystallized from benzene–alcohol. In the best large run (on 12 g. of crude low-melting diketone), the yield of light yellow 3′-methyl-1,2-benzanthracene (XIX) was 6.83 g. (61%), m. p. 162–163°. Using 0.85 g. of diol from pure high-melting diketone the product weighed 0.55 g. (73%); in several larger runs the yields were near 61% based on the crystalline diol and 54% based on the diketones. The best melting point of colorless plates, m. p. 163.0–163.9°,[19] was obtained after purification through the picrate, m. p. 146.0–146.8°,[19] chromatography over alumina and by recrystallization from ethanol–benzene.

From one run with sulfur a small amount of dihydro-3′-methyl-1,2-benzanthracene, colorless plates, m. p. 114.4–114.8°, was isolated from the more soluble fractions. The trinitrofluorenone derivative,[40] fine red needles, m. p. 237.5–239.5°, was obtained from benzene.

Anal. Calcd. for $C_{19}H_{16}$: C, 83.4; H, 6.6. Found[c]: C, 83.5, 83.5; H, 6.1, 6.4. Calcd. for $C_{32}H_{21}O_7N_3$: C, 68.7; H, 3.8; N, 7.5. Found[c]: C, 69.0, 68.8; H, 3.5, 3.6; N, 7.4, 7.5.

6-Methyl-1,2-benzanthracene.—The following synthesis was quite similar in most details to that already described for 3′-methyl-1,2-benzanthracene. *p*-Tolylacetic acid was prepared from *p*-methylacetophenone using the recommended ratio of reactants[41] and a twenty-two-hour refluxing time, the yield of thiomorpholide, m. p. 102–103°, being 56–58%. It was hydrolyzed to the acid in 84% yield. The crude product melted at 89–91° and was converted directly to the chloride (92%) with thionyl chloride. This distilled product was used in the Friedel–Crafts reaction with benzene, which was carried out as described above for benzyl *p*-tolyl ketone. The *p*-methylbenzyl phenyl ketone,[37] m. p. 92–95° after one recrystallization from alcohol, was formed in 88% yield.

The Stobbe condensation with this compound was quite similar to that already described, only sodium methoxide being investigated as a condensing agent. Crude diacid could be isolated from the reaction mixture in 45% yield, but reduction of the material remaining in solution indicated that the yield in the Stobbe reaction must have been at least 56%. The crude acid, XVa, was essentially pure; recrystallization from benzene–acetone gave colorless crystals, m. p. 172.6–174°.

Anal. Calcd. for $C_{19}H_{18}O_4$: C, 73.5; H, 5.9. Found[c]: C, 73.7, 73.8; H, 5.8, 5.8.

This compound was reduced as above[4] to yield 58% of a high-melting form, XVIa, m. p. 180–186°, from benzene, and 31% of the low-melting isomer, XVIa, m. p. 135–137°, from benzene–Skellysolve B. Only the former could be obtained in pure form by recrystallization from benzene, m. p. 189.5–190.5°. The colorless crystals melted with gas evolution.

Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.1; H, 6.5. Found[c]: C, 73.6, 73.5; H, 6.6, 6.5.

For cyclization, 24 g. of acid mixture, XVIa, was stirred into 350 ml. of anhydrous hydrogen fluoride in a silver cylinder. After standing until the reagent had evaporated, there was obtained 6.9 g. (33%) of a mixture of diketones, XVIIa, m. p. 165–172°, and 8.6 g. (38%) of a keto-acid, XXa, m. p. 209–211°. When a copper container was used for a larger run, the yield of diketones was about the same (35%) but the yield of keto-acid was less (21%) and of this a considerable amount was obtained only after digesting a dark insoluble copper-containing dark-red material with pyridine followed by dilution with water and acidification. All of the products from this run were dark colored but subsequent reactions proceeded satisfactorily. On recrystallization from benzene–acetone XXa was obtained as colorless crystals, m. p. 211.2–212.5°. No attempt was made to separate the isomeric diketones, XVIIa, m. p. 165–172°.

Anal. Calcd. for $C_{19}H_{18}O_3$: C, 77.5; H, 6.2. Found[c]: C, 77.5, 77.7; H, 6.0, 6.2.

In an attempt to effect ring closure omitting hydrogen

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[40] Orchin and Woolfolk, THIS JOURNAL, **68**, 1727 (1946).

[41] M. S. Newman, *J. Org. Chem.*, **9**, 521 (1944). See Carmack, "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1946, Vol. III, p. 104.

fluoride, 5.6 g. of high melting acid, XVIa, was heated at 140° with a solution of 13 g. of stannic chloride in 50 ml. of chlorobenzene. Only 1.2 g. of XXa was isolated from the resinous product.

The crude diketone mixture (38.1 g.) was reduced with lithium aluminum hydride as described above for the 3′-derivative in almost quantitative yield. The crude diol was not characterized but dehydrated by heating at 170–220° over several crystals of iodine. The resulting reaction product was treated with an equivalent of sulfur and heated from 160 to 250° for two hours. After chromatography in benzene over alumina there was obtained 20.2 g. (57%) of 6-methyl-1,2-benzanthracene m. p. 150–152°.

Application of the Clemmensen–Martin procedure to the reduction of XXa was unsatisfactory, 7.5 g. of the keto-acid giving 3.7 g. (52%) of crude reduced acid and 1.1 g. of recovered starting material. The product was recrystallized from benzene and then from Skellysolve B, to give colorless dense crystals of XXIa, m. p. 116.5–118°. It is suggested that the procedure to be described under 8-methyl-1,2-benzanthracene would prove superior for this reduction.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.4; H, 7.2. Found[e]: C, 81.4, 81.3; H, 7.1, 7.3.

This compound (3.1 g.) was added to about 50 ml. of anhydrous hydrogen fluoride, giving 2.4 g. (83%) of the ketone, XXIIa, m. p. 167–169°. Recrystallized from benzene–ethanol, the fine needles, m. p. 167.1–168.4°, sublimed *in vacuo* when dried at 100°.

Anal. Calcd. for $C_{19}H_{18}O$: C, 87.1; H, 6.9. Found[e]: C, 87.3, 87.3; H, 7.0, 7.1.

The corresponding alcohol was obtained in 96% yield (1.92 g., m. p. 155.5–157.5°) by application of the lithium aluminum hydride method to 2.0 g. of the ketone. It separated from benzene–ethanol in fine needles, m. p. 159.0–159.8°.

Anal. Calcd. for $C_{19}H_{20}O$: C, 86.3; H, 7.6. Found[e]: C, 86.1, 86.3; H, 7.8, 7.6 (analysis corrected for ash).

Dehydration of the alcohol (1.60 g.) in the presence of iodine at about 180°, followed by heating with the theoretical amount of sulfur at 250°, and distillation of the product *in vacuo*, gave 0.79 g. (54%) of 6-methyl-1,2-benzanthracene, light yellow plates of m. p. 147–149° (did not depress the melting point of an authentic sample).

8-Methyl-1,2-benzanthracene.—The required *o*-methylbenzyl phenyl ketone, m. p. 65–68°, b. p. 148–152° at 1 mm., was prepared in 70% yield by condensing *o*-tolylacetyl chloride and benzene using a procedure about the same as that used in preparing benzyl *p*-tolyl ketone above. A pure sample, m. p. 68.4–69.4°, was obtained from methanol.

Anal. Calcd. for $C_{15}H_{14}O$: C, 85.7; H, 6.7. Found[e]: C, 85.8, 86.0; H, 6.9, 6.8.

The Stobbe condensation was carried out in 62% yield using sodium methylate essentially as described above under the 3′-methyl derivative. The unsaturated acid, XVb, was purified from benzene–acetone to yield colorless crystals, m. p. 194.5–195.5° decomp.

Anal. Calcd. for $C_{19}H_{18}O_4$: C, 73.5; H, 5.9. Found[e]: C, 73.5, 73.4; H, 6.1, 5.8.

The mixture of saturated acids, XVIb, m. p. 156–165°, prepared by reduction with Raney alloy and alkali[4,31] as described above, was not separated into its components but was cyclized directly with hydrogen fluoride. From 12 g. of acids, XVIb, and 120 ml. of hydrogen fluoride there was obtained only 1.25 g. (12%) of a mixture of diketones, XVIIb, m. p. 184–220°, and 7.3 g. (65%) of a keto-acid, m. p. 194–196°, presumably XXb. On recrystallization from benzene–acetone XXb formed colorless crystals, m. p. 192.8–194.0°.

Anal. Calcd. for $C_{19}H_{18}O_3$: C, 77.5; H, 6.2. Found[e]: C, 77.4, 77.2; H, 6.1, 6.1.

In a large run (142 g. of XVIb in 1700 ml. of hydrofluoric acid, most of the hydrogen fluoride was removed by heating the copper flask at 30–35° under a stream of nitrogen. After adding about 2 l. of benzene and stirring, the mixture was poured on ice. On filtration and washing with water, 36.7 g. of insoluble diketones, m. p. 183–190°, was obtained. The keto-acid was extracted from the solvent layer with carbonate; distillation of the solvent gave an additional 18 g. of neutral solid (total diketones, 54.7 g., 44%). The acid separated from benzene as a brown powder, m. p. 193–195°, total 47.5 g. (36%, total conversion 80%). This method eliminated the formation of copper-containing solids previously mentioned.

The diketones, XVIIb (54.7 g.), were reduced with excess lithium aluminum hydride as described above. The oven-dried crude brown diol was dehydrated at 180 to 225° for thirty minutes, an equivalent of sulfur was added, and heating resumed at 240–250° for a like period. The hydrocarbon was purified by distilling from zinc *in vacuo*, chromatography over alumina in benzene, recrystallization from benzene–ethanol. The mixture of light yellow needles and prisms (24.4 g., 51% yield) melted at 116–118°.

The application of Clemmensen reduction to XXb using 3.4 g. of acid in 70 ml. of acetic acid with 50 g. of amalgamated granulated zinc, and adding a mixture of 25 ml. of hydrochloric acid and 70 ml. of acetic acid, gave 2.72 g. (84%) of XXIb, m. p. 136–140°, which separated from benzene–Skellysolve C as a white powder, m. p. 142.7–144.2°.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.4; H, 7.2. Found[e]: C, 82.0, 81.9; H, 7.4, 7.3.

The modified Wolff–Kishner procedure gave only tars with XXb.

The acid XXIb (2.2 g.) was added to about 50 ml. of anhydrous hydrogen fluoride to give 1.40 g. (68%) of the ketone, XXIIb, m. p. 163–165°. On recrystallization from benzene–ethanol XXIIb separated as colorless platelets, m. p. 164.1–164.9°.

Anal. Calcd. for $C_{19}H_{18}O$: C, 87.0; H, 6.9. Found[e]: C, 87.2, 86.9; H, 7.0, 7.1.

Lithium aluminum hydride reduction gave the corresponding alcohol in quantitative yield, m. p. 161–164°. White needles were obtained from methanol, m. p. 164.5–165.2°.

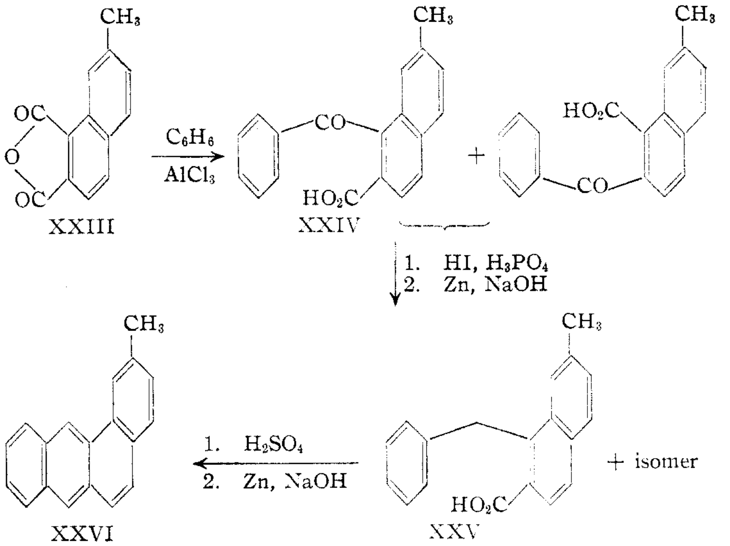
Anal. Calcd. for $C_{19}H_{20}O$: C, 86.3; H, 7.6. Found[e]: C, 86.5, 86.8; H, 7.7, 7.6.

In the usual way, 0.90 g. of this compound yielded 0.36 g. (42%) of 8-methyl-1,2-benzanthracene as yellow prisms, m. p. 117–118° (partially as the picrate, flat red needles, m. p. 157–159°). The purest sample melted at 117.4–118.4° and after solidifying remelted at 113.4–114.0° in agreement with the behavior previously noted.[8a]

2′-Methyl-1,2-benzanthracene.—A new synthesis of this compound has been developed. 7-Methyl-1,2-naphthalic anhydride, XXIII, was prepared from ethyl γ-*p*-tolylbutyrate by the same procedure developed for the unmethylated analog.[26] The anhydride was condensed with benzene to yield a mixture of benzoylnaphthoic acids, XXIV, which was reduced by the two-step (hydriodic–phosphoric in acetic followed by zinc dust and alkali) reduction process previously mentioned to a mixture of benzylnaphthoic acids, XXV. Ring closure and reduction afforded the desired hydrocarbon, XXVI. The reactions are outlined in the chart.

Ethyl γ-*p*-tolylbutyrate was converted into 7-methyl-3,4-dihydro-1,2-naphthalic anhydride, m. p. 137.5–139.5°, in 57–60% yields (in large batches) essentially as described by Fieser and Hershberg.[26] The pure dihydroanhydride, light yellow needles from benzene, melted at 143.4–144.4°.

Anal. Calcd. for $C_{13}H_{10}O_3$: C, 72.9; H, 4.7. Found[k]: C, 72.9, 73.2; H, 4.9, 4.9.



When 153.5 g. of the dihydroanhydride was heated with one equivalent of sulfur at 250° for three hours and at 270° for four hours, there was obtained 116.7 g. (76.7%) of 7-methyl-1,2-naphthalic anhydride, XXIII, m. p. 162–164.6°. A pure sample, obtained by refluxing with sodium carbonate, acidifying, dehydrating the acid to the anhydride by heating at 210° and recrystallizing from benzene, melted at 166.4–167.4° and gave no test for sulfur.

Anal. Calcd. for $C_{13}H_8O_3$: C, 73.6; H, 3.8. Found[k]: C, 73.7, 73.9; H, 4.1, 4.0.

The Friedel–Crafts reaction of 7-methyl-1,2-naphthalic anhydride with benzene was complicated by the insolubility of the anhydride in the hydrocarbon, which prevented the use of low temperatures. In one run, at room temperature, 50% of the anhydride was recovered unchanged, only a small yield of keto-acids being obtained. At higher temperatures, the formation of a neutral by-product, presumably a diphenyl-7-methyl-1,2-naphthalide, was a serious competing reaction. When the amount of benzene was reduced and the reaction carried out in *o*-dichlorobenzene no improvement was noted. The following experiment represents the highest conversion to keto-acids obtained.

Five grams of the anhydride was dissolved in 100 ml. of reagent benzene by refluxing briefly. The flask containing the solution was placed in an oil-bath maintained at 50°. When the temperature had dropped to that of the bath, 7.4 g. of reagent anhydrous aluminum chloride was added in portions and stirring was continued for ninety minutes. The mixture was decomposed as usual and the precipitated products taken up in ether. The solution was extracted with sodium carbonate and the extracts acidified; the oil solidified and was ground, washed and dried. The light yellow keto-acids, XXIV, weighed 4.27 g. (62%) and melted at about 190–215°. In a large run conducted in this manner, 107 g. of anhydride gave 84 g. (58% yield) of keto-acids and the neutral fraction yielded 43 g. (24%) of the aforementioned yellow phthalide, m. p. 195–200°. A sample was recrystallized from benzene, giving white crystals, m. p. 199.6–200.6°. It was recovered unchanged from attempted hydrolysis with alcoholic sodium hydroxide, followed by treatment with zinc dust–aqueous alkali.

Anal. Calcd. for $C_{25}H_{18}O_2$: C, 85.7; H, 5.2. Found[k]: C, 86.0, 85.6; H, 5.2, 5.1.

No attempts were made to separate the pure isomers, XXIV, and subsequent steps were carried through with mixtures.

The lactones were obtained by the phosphorus–hydriodic acid procedure already described in connection with the synthesis of 5-methyl-1,2-benzanthracene. The mixture melted at 310–340° uncor. and was reduced as usual to the benzyl-type acids, m. p. 100–140°. In the best run, 84 g. of keto-acids gave 64 g. (80%) of reduced acids, XXV. Closure of this mixture (33 g.) with sulfuric acid and reduction of the anthrone yielded 16.8 g. (58%) of 2′-methyl-1,2-benzanthracene as light yellow crystals, m. p. 148.5–150.0°, from ethanol–toluene. Working up the toluene layer from the last reduction separately from the acetone extracts of the zinc proved advantageous in that colorless opaque needles, m. p. 150.7–151.7°,[19] were obtained by two recrystallizations from ethanol–benzene.

Unsuccessful experiments on the keto-acids included a benzoyl chloride–sulfuric acid closure, which gave principally soluble products. The acid, XXIV, was also converted to the chloride (phosphorus pentachloride in benzene) and the solid compound heated to 180° without apparent change. An attempted Friedel–Crafts closure of the chloride (aluminum chloride in carbon disulfide at room temperature) gave a small amount of very high-melting material which was not investigated.

Attempts to improve the conversion of the intermediate benzanthrones to XXVI by adopting reduction other than by zinc dust–sodium hydroxide were made: a phosphorus–hydriodic acid reduction in acetic acid yielded no crystalline pure product; reduction with ethereal lithium aluminum hydride afforded only a 33% yield of slightly impure product.

9-Methyl-1,2-benzanthracene.—The synthesis of this compound involved the ring closure of *o*-[α-1-naphthylethyl]-benzoic acid, XXVII, by a zinc chloride fusion to the anthrone[42] followed by zinc dust and alkali reduction to the hydrocarbon.

In the best run, an intimate mixture of 32 g. of XXVII and 100 g. of powdered fused zinc chloride was held for twenty minutes in a tube in a salt-bath at 180°. After cooling first to room temperature and then by Dry Ice the tube was broken and the glassy cake triturated in a cold mortar with ice and hydrochloric acid. The solid was collected rapidly and the process repeated. If the solid became gummy the yield was less. After washing the crude anthrone with ice-water and cold sodium carbonate solution, the anthrone was reduced by the zinc dust–sodium hydroxide method to yield, after crystallization from alcohol–benzene, 21 g. (75%) of pale yellow crystals, m. p. 137.5–139.0°, of hydrocarbon. After purification by recrystallization of the picrate the melting point was raised to 138.6–139.6°.[19]

The acid, XXVII, was recovered unchanged after heating with a mixture of sulfuric and phosphoric acids at 40°. Attempts to reduce 10-acetoxy-9-methyl-1,2-benzanthracene[43] with zinc dust–sodium hydroxide in the presence of toluene, with aluminum isopropoxide or with lithium aluminum hydride were unsuccessful. A low yield (24%) of pure 9-methyl-1,2-benzanthracene, m. p. 138–139°, was obtained by an alkaline aqueous dioxane hydrolysis of this acetate, followed by the usual zinc dust alkali reduction.

9,10-Dimethyl-1,2-benzanthracene.—This compound was prepared by iodomethylation.[44] The use of paraformaldehyde in place of chloromethyl ether in the iodomethylation step is described below.

A solution of 2.3 g. of paraformaldehyde in 13.8 ml. of 47% hydriodic acid and 10 ml. of acetic acid was added to a solution of 0.25 g. of 9-methyl-1,2-benzanthracene in 10 ml. of acetic acid. After standing at 5–10° for one hour 0.35 g. (90%) of 10-iodomethyl-9-methyl-1,2-benzanthracene[45] was obtained.

Summary

New syntheses for 3-, 6-, 7-, 8-, 2′- and 3′-methyl-1,2-benzanthracene are described as well

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[42] J. W. Cook, A. M. Robinson and F. Goulden, *J. Chem. Soc.*, 393 (1937).

[43] M. S. Newman, THIS JOURNAL, **60**, 1141 (1938).

[44] R. B. Sandin and L. F. Fieser, *ibid.*, **62**, 3098 (1940).

as improvements on previously reported syntheses of the 4-, 5- and 9-isomers. 1,2-Benzanthracene, 10-methyl- and 9,10-dimethyl-1,2-benzanthracene have also been prepared. At least 25 g. of each compound has been made so that these compounds may be made available to cancer research workers.

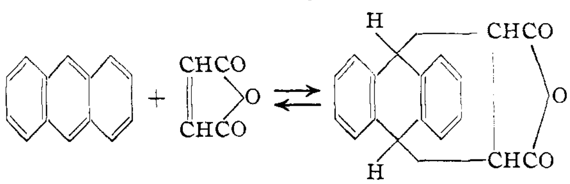
COLUMBUS 10, OHIO RECEIVED SEPTEMBER 6, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

Polymethyl Aromatic Hydrocarbons. III. The Reaction of 1,2,3,4-Tetramethylnaphthalene with Maleic Anhydride[1]

BY MILTON C. KLOETZEL,* RHODES P. DAYTON AND HERSHEL L. HERZOG[2]

Diels and Alder[3] demonstrated the existence of a dienoid system in the *meso* ring of anthracene by effecting a reaction of this hydrocarbon with maleic anhydride to yield 9,10-dihydroanthracene-9,10-endo-α,β-succinic anhydride (I).



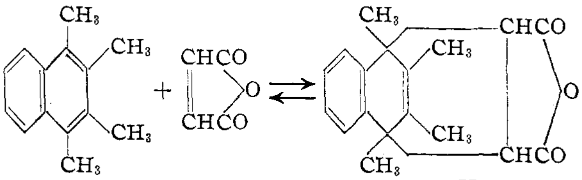
I

Bachmann and Kloetzel[4] later demonstrated the reversible nature of the reaction between maleic anhydride and polycyclic hydrocarbons containing the anthracene nucleus, and also discovered that the presence of methyl groups in the *meso*-positions of anthracene greatly facilitated this reaction. Thus, the reaction of equimolar quantities of maleic anhydride and 9,10-dimethylanthracene in refluxing benzene was 95% complete within five minutes, whereas anthracene itself required seven and seven-tenths hours for 96% reaction under these conditions.

Despite the formal analogy between anthracene and naphthalene, the latter hydrocarbon has been reported[5] not to undergo a reaction with maleic anhydride, even after prolonged refluxing in toluene.[6] Dienoid character in naphthalene is manifested, however, in certain other of its reactions. For example, reduction with sodium and alcohol yields 1,4-dihydronaphthalene.[7] Naphthalene also forms 1,4-organometallic addition products with lithium[8] or sodium[9] in ether.

Consideration of the activating influence of methyl groups upon the anthracene nucleus suggested the possibility that a Diels–Alder type reaction with the naphthalene nucleus might become feasible if enough methyl groups were substituted on one ring of naphthalene to enhance the potential dienoid character of that ring.

Such a reaction now has been effected. A 90% yield of adduct (II) was obtained when 1,2,3,4-tetramethylnaphthalene was treated with a large excess (30 moles) of maleic anhydride in refluxing benzene. To our knowledge, this is the first instance in which a dienoid system wholly within the naphthalene nucleus has been observed to undergo a Diels–Alder reaction. The reaction is remarkable in that a resonance-stabilized aromatic system is disrupted under such mild conditions and illustrates the profound modifying influence which methyl groups can exert upon such a system.



II

The reaction of 1,2,3,4-tetramethylnaphthalene with maleic anhydride was shown to be reversible. The equilibrium yield of adduct, obtained within forty-six hours, from equimolar quantities of hydrocarbon and maleic anhydride in boiling xylene was 4.6–6.4%. Prolonged heating did not increase the yield of adduct. The position of equilibrium was checked by recovering the hydrocarbon produced upon dissociation of the pure adduct in boiling xylene solution. It is evident that equilibrium in boiling xylene is less favorable for the production of adduct from 1,2,3,4-tetramethylnaphthalene than it is from 9,10-diphenylanthracene, which gives the poorest yield (16%) of any anthracene derivative reported by Bachmann and Kloetzel.[4] In spite of this fact, it is possible to obtain an excellent yield (90%)

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[1] Abstracted from the thesis submitted by Rhodes P. Dayton, and a portion of the dissertation submitted by Hershel L. Herzog to the Graduate School of the University of Southern California in partial fulfillment of the requirements for the degrees of Master of Science and Doctor of Philosophy, respectively. Presented before the Division of Organic Chemistry, San Francisco, March, 1949.

[2] Standard Oil Company of California Graduate Fellow in Chemistry.

[3] Diels and Alder, *Ann.*, **486**, 191 (1931).

[4] Bachmann and Kloetzel, THIS JOURNAL, **60**, 481 (1938).

[5] Mameli, Pancotto and Crestani, *Gazz. chim. ital.*, **67**, 669 (1937).

[6] We have found that even when naphthalene is fused with 30 moles of maleic anhydride at 100° for twenty-four hours, reaction occurs to the extent of less than 1%. This reaction will be described in a forthcoming communication.

[7] Bamberger and Lodter, *Ber.*, **26**, 1833 (1893); Straus and Lemmel, *ibid.*, **46**, 232 (1913); Straus, *ibid.*, **46**, 1051 (1913); Straus and Lemmel, *ibid.*, **54**, 25 (1921).

[8] Schlenk and Bergmann, *Ann.*, **463**, 1 (1928).

[9] Hückel and Bretschneider, *ibid.*, **540**, 157 (1939).