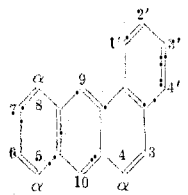
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Synthesis of 4,9- and 4,10-Dimethyl-1,2-benzanthracenes[1]

BY LOUIS F. FIESER AND R. NORMAN JONES[2]

Of the ten known dimethylbenzanthracenes those which have shown the most interesting behavior in tests for carcinogenic activity carry substituents in either a meso- or an α-position of the anthracene nucleus. Such substitution is



lacking in the 2′,6-, 2′,7-, 3′6-, 3′,7-, and 6,7-dimethyl derivatives,[3] and tests of the hydrocarbons by application to the skin of mice[4] have shown that the first four compounds are inactive and that the 6,7-dimethyl derivative is but weakly carcinogenic. On the other hand, the 5,6-dimethyl isomer[5] is a moderately rapidly acting carcinogen[4] comparable with 1,2,5,6-dibenzanthracene, the 5,9-isomer[6] and the 5,10-derivative[7] are about equal in potency to methylcholanthrene as sarcoma-producing agents, and the 9,10-dimethyl compound[8] is a highly active carcinogen.[9] 1′,10-Dimethyl-1,2-benzanthracene[10] has a substituent in the favorable meso position 10, but the presence of the 1′-methyl group seems to result in decreased activity, for the hydrocarbon has given no subcutaneous tumors in six months.[9] Although it is too early to formulate any but tentative conclusions, the results on record suggest that there is an interesting reinforcing effect of methyl groups in the *meso*- and α-positions. As a means of determining to what extent this effect may be general, it seemed desirable to add to the list of known dimethyl-1,2-benzanthracenes further compounds meeting the specifications indicated. The 4,9- and 4,10-dimethyl derivatives are of particular interest not only because of these considerations but because of the relationship of the former compound to 4,10-ace-1,2-benzanthracene,[11,12] which has been found to give tumors in rats[13] and in mice[14] (Shear[9]), in the latter case in remarkably small dosage.

The scheme of synthesis employed was selected for investigation partly because it offered the possibility of obtaining not only the aromatic hydrocarbons in question but their 1′,2′,3′,4′-tetrahydro derivatives. These seemed of interest in connection with studies in progress on other hydroaromatic derivatives of carcinogens,[15] and since the work was started Shear[9] has made the interesting observation that 1′,2′,3′,4′-tetrahydro-4,10-ace-1,2-benzanthracene[11] has marked carcinogenic activity, giving added significance to the corresponding tetrahydro-4,10-dimethyl compound.

The plan of synthesis is indicated in the chart and involves the introduction of a methyl group at the 4-position by the use of 6-methyltetralin (I) as a component in a phthalic anhydride synthesis. By applying to the intermediate keto acid II the synthetic operations introduced by Fieser and Newman[7] in one series (a) and those of Fieser and Hershberg[16] in another (b), it was possible to introduce methyl groups at positions 10 and 9, respectively. 6-Methyltetralin was synthesized by Krollpfeiffer and Schäfer[17] from toluene and succinic anhydride, and a hydrocarbon of similar boiling point was obtained by Schroeter[18] by the high-pressure hydrogenation of β-methylnaphthalene. As an indication of the structure of the hydrocarbon, Schroeter observed that the keto acid (II) resulting from the condensation of the substance with phthalic acid yielded a single anthraquinone on cyclization, whereas the corresponding acid from tetralin affords two isomers. The difference was attributed to the blocking action of the methyl group, and hence it was inferred that the substituent is contained

(1) This investigation was conducted as part of a program of research receiving support from the National Cancer Institute.

(2) Commonwealth Fund Fellow.

(3) Cook, *J. Chem. Soc.*, 456 (1932).

(4) Cook, *Proc. Roy. Soc.* (London), **B111**, 485 (1932); Barry, *et al.*, *ibid.*, **B117**, 318 (1935).

(5) Cook and Haslewood, *J. Chem. Soc.*, 428 (1937).

(6) Newman, THIS JOURNAL, **59**, 1003 (1937).

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

(8) Bachmann and Chemerda, *ibid.*, **60**, 1023 (1938); Newman, *ibid.*, **60**, 1141 (1938).

(9) Shear, publication in press.

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

(11) Fieser and Seligman, *ibid.*, **59**, 883 (1937).

(12) Dansi, *Gazz. chim. ital.*, **67**, 85 (1937).

(13) Morelli and Dansi, *Biochimica e terapia sper.*, **24**, 432 (1937).

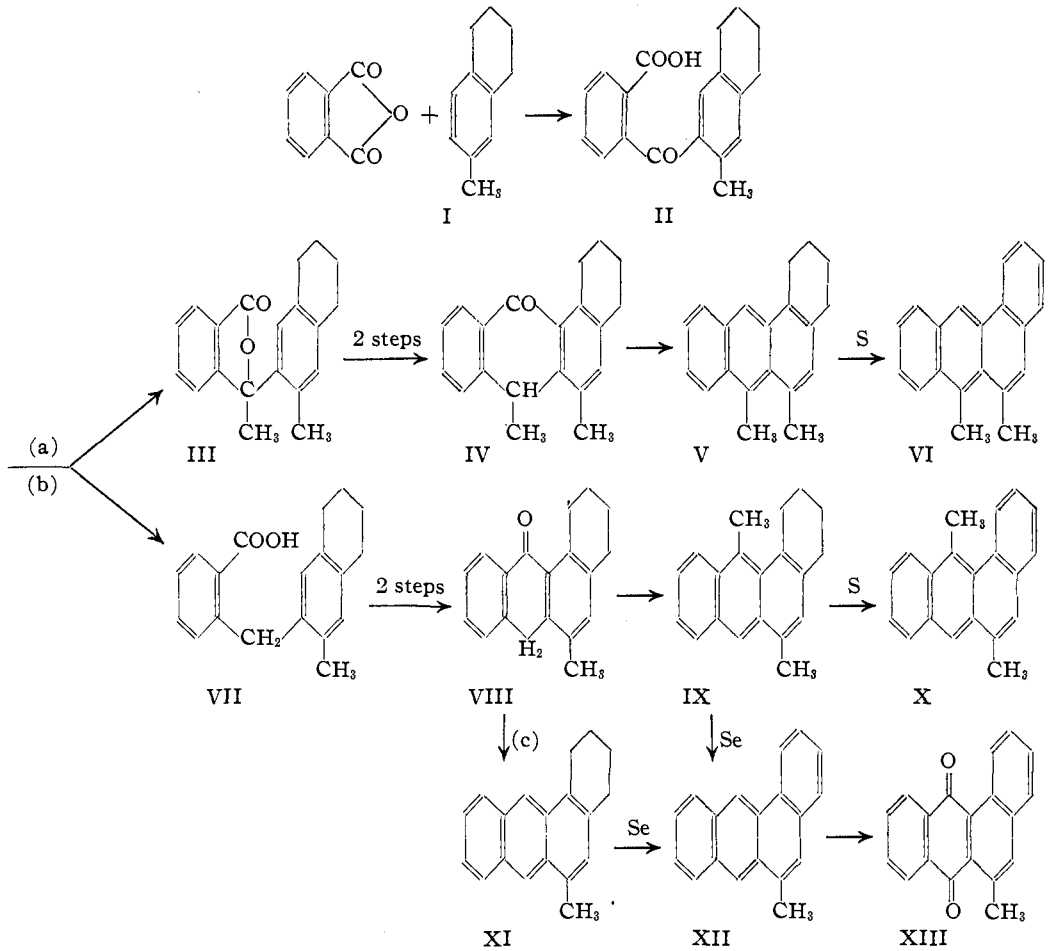
(14) Fieser and Campbell, THIS JOURNAL, **60**, 1142 (1937).

(15) Fieser and Hershberg, *ibid.*, **59**, 2502 (1937); **60**, 940 (1938).

(16) Fieser and Hershberg, *ibid.*, **59**, 1028 (1937).

(17) Krollpfeiffer and Schäfer, *Ber.*, **56**, 620 (1923).

(18) Schroeter, *ibid.*, **54**, 2242 (1921).



in the aromatic ring. In the present work this keto acid (II) was prepared from hydrocarbon obtained by hydrogenation and put through the steps of series (b) and (c) and thus converted into a product identical with a sample of the known 4-methyl-1,2,benzanthraquinone,[19] and the hydrocarbon XII and its picrate corresponded in properties with the descriptions given by Cook.[20] This evidence confirms the conclusion reached by Schroeter but does not distinguish between positions 7 and 8 as possible points of attachment of the phthalic acid residue in 6-methyltetralin. In order to settle the matter the keto acid was oxidized exhaustively with dilute nitric acid, and the sublimed product was found to be identical with pyromellitic anhydride. This proves that the structure II is correct and that 6-methyltetralin undergoes substitution at the 7-position. Since the yield of pure keto acid in the Friedel and Crafts reaction was low (42%) and the crude material contaminated with a considerable amount of other acidic products, it is possible that the material obtained by the hydrogenation of β-methylnaphthalene does not consist entirely of pure 6-methyltetralin but contains other hydro derivatives.

No difficulties were encountered in carrying the two series of syntheses to the stage of the isomeric dimethyltetrahydrobenzanthracenes, V and IX. The anthrone IV was obtained by cyclizing the reduction product of the lactone III with sulfuric acid and was isolated easily in a pure condition in the stable ketonic form. Acetylative cyclization[16] of the acid VII with zinc chloride catalyst gave an anthranyl acetate, and when this was cleaved with a Grignard reagent the enol liberated isomerized to the more stable keto form VIII in the process of recovery and purification. With respect to the relative stability of the keto and enol forms, 4-methyl- and 4,10-dimethyl-1',2',3',4'-tetrahydro-1,2-benz-10-anthrone, like the unmethylated compound,[21] con-

(19) Fieser and Peters, THIS JOURNAL, **54**, 3742 (1932).
(20) Cook, *J. Chem. Soc.*, 1592 (1933).
(21) Fieser and Hershberg, THIS JOURNAL, **59**, 2331 (1937).

form to the behavior noted for anthrone[21] rather than for 1,2-benz-10-anthrone.[16] In series (b) this was of advantage in facilitating the introduction of the 9-methyl group by a Grignard reaction.

The dehydrogenation of the tetrahydrides V and IX presented considerable difficulty, apparently because of the ready elimination of an alkyl group from a meso position of the 1,2-benzanthracene molecule. The dehydrogenation of the 4,9-dimethyl compound (IX) was tried first and when selenium was used the only reaction product which could be isolated in a satisfactory condition proved to be identical with the sample of 4-methyl-1,2-benzanthracene (XII) prepared from its tetrahydride with the use of selenium. It may be recalled that a similar loss of a *meso* (10)-isopropyl group has been noted in this Laboratory[16,21] in a dehydrogenation with selenium but that with sulfur the group was retained. It is also of interest that in a selenium dehydrogenation investigated by Cook[20] an isopropyl group was lost from the α-position 5. A methyl group in the α-position 4 seems to withstand treatment with selenium, at least in part, although the yield of the pure 4-methyl compound was never good. Since selenium was found unsatisfactory for the dehydrogenation of the dimethyl compounds, and as trial experiments with palladium charcoal seemed unpromising, sulfur eventually was employed. In each case the product was a hydrocarbon mixture, but on careful purification through the picrate or trinitrobenzene derivative it was possible to isolate an apparently homogeneous hydrocarbon having the composition required for a dimethyl-1,2-benzanthracene. The two hydrocarbons differ considerably in melting point and in the melting points of their derivatives and they are easily distinguishable, by analysis and properties, from the 4-methyl compound. Although the yields in the last step were quite low, the desired end was achieved and samples of 4,9- and 4,10-dimethyl-1,2-benzanthracene sufficient for tests of possible carcinogenic activity were obtained.

Experimental Part[22]

6-Methyltetralin (I).—Commercial β-methylnaphthalene was freed from sulfur by distillation from sodium at atmospheric pressure, and 100 g. of the purified hydrocarbon, mixed with 20 cc. of absolute alcohol, was hydrogenated in the presence of Raney nickel catalyst (5 cc. of the suspension) at an initial pressure of 1800 lb. (120 atm.) and a temperature of 130–135°. The reaction was stopped after the absorption of two moles of gas and the product was combined with that from a second batch and fractionated at atmospheric pressure through a 1-meter column. The chief fraction (96 g.) distilled at 222–226° (n^{20}D 1.5328), and a second fraction (44 g.) boiled at 226–227° (n^{20}D 1.5350); total yield, 68%.

o-**(6-Methyl-7-tetraloyl)-benzoic Acid (II).**—Schroeter[18] prepared this acid in unspecified yield using benzene as the solvent. In our procedure a solution of 63 g. of 6-methyltetralin and 63 g. of phthalic anhydride in 500 cc. of tetrachloroethane was cooled to 0° and 120 g. of aluminum chloride was added with stirring in two and one-half hours while cooling in an ice-bath. After decomposition with ice and acid and removal of the solvent with steam, the solidified product in 800 cc. of 10% sodium carbonate solution was submitted to steam distillation, precipitated with acid, coagulated by boiling, collected and washed. The crude product (124 g., m. p. 135–140°) on crystallization from glacial acetic acid afforded 53 g. (42%) of colorless acid melting at 165–167°. A sample recrystallized to constant melting point from carbon tetrachloride formed small needles, m. p. 167.5–168° (Schroeter, 160°, uncorr.). It was evident that the crude reaction product contained considerable amounts of other acids. Schroeter isolated the acid II in the form of the ammonium salt and, while we found this a less satisfactory method of obtaining the acid in a pure condition than that adopted, use was made of partial purification through the ammonium salt to provide material suitable for reduction.

For proof of structure 1 g. of the keto acid was heated with 2 cc. of nitric acid (sp. gr. 1.42) and 4 cc. of water at 200–210° for one day; a fresh 2-cc. portion of concentrated acid was introduced and heating was continued for fifteen hours. After concentrating the solution, fuming acid precipitated a solid which was dried and sublimed at 250° and 15 mm. Recrystallized twice from dioxane and dried at 150° to remove solvent of crystallization, the product melted at 282–284° and gave no depression with a sample of authentic pyromellitic anhydride which had been freshly sublimed and crystallized and which melted at 283–285°.[23]

Series (b)

o-**(6-Methyl-7-tetralylmethyl)-benzoic Acid (VII).** (a) **From Purified Keto Acid.**—The acid II (2 g., m. p. 164.5–165.5°) was heated with zinc dust (2 g.) and 2 *N* sodium hydroxide solution (50 cc.) for forty-eight hours on the steam-bath and after acidification the reaction product was extracted with ether, taken into soda solution, precipitated, and crystallized from methanol, giving 1.45 g. (76%) of long, white needles, m. p. 168.5–168.9°. After recrystallization the m. p. was 168.9–169.1°.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.04; H, 7.19. Found: C, 81.48; H, 7.12.

(b) **From the Crude Ammonium Salt.**—The crude product (59 g.) of the Friedel and Crafts reaction from 32 g. of 6-methyltetralin was dissolved in 500 cc. of hot 1 *N* ammonia solution, and after clarification with Norite the

(22) All melting points are corrected. Analyses by Mrs. Verna R. Keevil, Dr. C. Fitz, and the Arlington Laboratories.

(23) Observation of Dr. E. B. Hershberg; this value is believed to be more reliable than that reported previously by Fieser and Hershberg, THIS JOURNAL, **57**, 2196 (1935).

filtrate was treated with ammonium chloride and cooled to 0°. The ammonium salt of II separated in a crystalline condition and weighed 52 g. (the acid liberated from this material is impure). A mixture of this salt with 52 g. of zinc dust and 1 liter of 2 *N* sodium hydroxide solution was refluxed gently with mechanical stirring for twenty-four hours and the solution, filtered through sintered glass, was acidified with dilute hydrochloric acid. The crude precipitate (45 g.) on crystallization from methanol gave 22 g. of acid, m. p. 166.5–167.5°, and 4.5 g., m. p. 161.5–163.5°. The yield from 6-methyltetralin was 43%, as compared with an over-all yield of 32% via the purified acid.

1',2',3',4' - Tetrahydro - 4 - methyl - 1,2 - benzanthranyl-9-acetate.—The acid VII (3.5 g.) was refluxed for one and one-half hours with glacial acetic acid (21 cc.), acetic anhydride (14 cc.) and anhydrous zinc chloride (0.28 g.) and sufficient water was added carefully to the pale yellow solution to produce faint cloudiness. On cooling there separated 3.4 g. (89%) of long, pale yellow needles, m. p. 148–149°. Recrystallization from acetic acid raised the melting point to 150.5–151°.

Anal. Calcd. for $C_{21}H_{20}O_2$: C, 82.86; H, 6.62. Found: C, 82.40; H, 6.45.

1',2',3',4' - Tetrahydro - 4 - methyl - 1,2 - benz - 9-anthrone (VIII).—The above acetate (6.5 g.) was refluxed for one hour in ether–benzene with the Grignard reagent from 11 g. of *n*-butyl bromide, and after hydrolysis the extracted product was crystallized from benzene–petroleum ether, giving colorless, non-fluorescent needles; yield, 5.54 g. (97%). Recrystallization raised the melting point slightly (0.5°) to 151.5–151.7°.

Anal. Calcd. for $C_{19}H_{18}O$: C, 86.98; H, 6.91. Found: C, 86.85; H, 6.81.

1',2',3',4' - Tetrahydro - 4,9 - dimethyl - 1,2 - benzanthracene (**IX**).—The anthrone VIII (3.75 g.) dissolved in benzene was added to the Grignard reagent formed by action of excess methyl chloride on 1 g. of magnesium. A deep red color developed and faded to yellow as the mixture was refluxed for one and one-half hours. After the addition of dilute acid to the cooled solution the organic layer (fluorescent) was washed and concentrated. The oily residue crystallized from methanol on seeding with a crystal previously obtained by the decomposition of the purified picrate (see below), giving 3.26 g. (88%) of small, pale yellow plates, m. p. 57–58°.

For the preparation of a pure sample, 2 g. of oily material in alcohol was treated with 2 g. of picric acid, yielding 2.5 g. of dark reddish-black needles of the **picrate**, m. p. 135.8–136.2° (1.65 g.).

Anal. Calcd. for $C_{20}H_{20}\cdot C_6H_3O_7N_3$: N, 8.59. Found: N, 8.83.

On decomposition of the picrate by chromatographic adsorption on activated alumina from benzene, the colorless, fluorescent filtrate on evaporation of the solvent and crystallization of the residue from methanol gave 0.65 g. of pale yellow plates of the hydrocarbon, m. p. 62.4–62.8°.

Anal. Calcd. for $C_{20}H_{20}$: C, 92.26; H, 7.74. Found: C, 92.55; H, 7.54.

Dehydrogenation of IX. (a) **With Sulfur: 4,9-Dimethyl-1,2-benzanthracene.**—A mixture of 500 mg. of the tetrahydride and 100 mg. of sulfur was heated slowly in a salt-bath in a stream of nitrogen. Evolution of hydrogen sulfide commenced at 180° and the mixture was maintained at 180–210° until liberation of this gas was complete (about four hours). The product was then distilled at 2 mm. pressure, yielding a ruby-red distillate which failed to crystallize from methyl or ethyl alcohol or to form a crystalline picrate. After passing a benzene solution of the oil through a tower of alumina there was obtained a light yellow oil which likewise failed to crystallize but which when dissolved in methanol with 300 mg. of trinitrobenzene yielded 135 mg. of long, bright red needles melting at 124.2–124.8°. The melting point of the complex remained unchanged on recrystallization, and by careful working of the mother liquors 195 mg. of satisfactory material was collected. This was adsorbed from benzene onto activated alumina, the trinitrobenzene being retained as a crimson zone at the top of the tower and the hydrocarbon forming a colorless zone having a blue fluorescence. After sectioning the tower this zone was eluted with benzene containing 5% methanol, and a solution of the pale yellow, oily residue in methanol slowly deposited small, faintly yellow needles, m. p. 73.3–74.3°; yield, 42 mg. (8.5%). Concentration of the mother liquors gave 13 mg., m. p. 69–71°. Recrystallization of the best material from methanol gave hydrocarbon melting at 75.1–75.5°. The picrate forms deep bronze colored needles, m. p. 116–116.4°, from methanol.

Anal. Calcd. for $C_{20}H_{16}$: C, 93.70; H, 6.30. Found: C, 93.68; H, 6.61.

(b) **With Selenium.**—The tetrahydride IX (800 mg.) was heated with 1.1 g. of selenium in a salt-bath at 300° for twenty-one hours, with the further addition of 1 g. of selenium in the course of the reaction. The product was extracted with boiling benzene and the solution was clarified by refluxing with metallic sodium and by two passages through activated alumina. Removal of the solvent and crystallization from methanol gave 350 mg. (44%) of 4-methyl-1,2-benzanthracene in the form of rosets of needles, m. p. 117.5–118.5°. Repeated crystallization from methanol raised the m. p. to 122.8–123.4°, and the sample gave no depression when mixed with the hydrocarbon prepared as described below. The picrate melts at 148–148.5°.

Series (c)

1',2',3',4' - Tetrahydro - 4 - methyl - 1,2 - benzanthracene (**XI**).—A mixture of 2 g. of the anthrone VIII, 10 cc. of toluene, 5 g. of zinc dust, and 100 cc. of 2 *N* sodium hydroxide was refluxed for forty-eight hours, with the further addition of 5 g. of zinc dust. The progress of the reduction was indicated by the development of blue fluorescence under ultraviolet light. The cooled reaction mixture was extracted repeatedly with benzene, and the solution was washed with acid and water and evaporated. The residue on crystallization from methanol afforded 1.1 g. (58%) of faintly yellow crystal clusters, m. p. 81.3–82.3°, and the mother liquors yielded 0.17 g. of material, m. p. 78–79°. Repeated crystallization from methanol–benzene gave faintly yellow clusters of needles, m. p. 82.3–82.9°. The picrate crystallized from methanol as deep reddish-brown needles, m. p. 158–158.2°.

Anal. Calcd. for $C_{19}H_{18}$: C, 92.63; H, 7.37. Found: C, 92.34; H, 7.61.

4-Methyl-1,2-benzanthracene.—Dehydrogenation of the tetrahydride XI (730 mg.) was accomplished by heating with selenium (2.1 g., added in portions) at 290–300° for twenty hours. The product, obtained by extraction with benzene and clarification with the use of sodium and an adsorption tower, was crystallized from methanol and gave 170 mg. (24%) of small, pale yellow needles, m. p. 119–120°. Repeated crystallization from alcohol–benzene gave material melting constantly at 124.1–124.6°.

Anal. Calcd. for $C_{19}H_{14}$: C, 94.18; H, 5.82. Found: C, 94.33; H, 5.61.

Cook[20] found the melting point 124.5–125.5° for the hydrocarbon and 149–150° for its picrate. The picrate prepared from the above sample formed brown-red needles, m. p. 148.5–149°; the trinitrobenzene derivative formed bright red needles, m. p. 163.5–164°. Oxidation of the hydrocarbon (29 mg.) with chromic anhydride in acetic acid at 60° gave, after crystallization from benzene–ligroin, 7 mg. of 4-methyl-1,2-benzanthraquinone, m. p. 167.5–168°, giving no depression when mixed with the sample prepared by Fieser and Peters.[19]

Series (a)

Lactone of 2-(α-Hydroxy-6,α-dimethyl-7-tetralylmethyl)-benzoic Acid (III).—A solution of 15 g. of o-(6-methyl-7-tetraloyl)-benzoic acid (II) in benzene was added to the Grignard solution from 4.8 g. of magnesium and excess methyl chloride in 100 cc. of ether. The solution became greenish-yellow and an oil deposited on the walls of the flask. After adding more benzene the mixture was refluxed for one and one-half hours, decomposed, and the product taken into benzene–ether. An amorphous white precipitate often separated at this point at the interface but eventually dissolved on vigorous shaking. In one experiment the solid was collected and found to be a magnesium complex which on being refluxed with methanol gives a flocculent precipitate and a solution containing the pure lactone. After washing the benzene–ether solution with sodium carbonate solution, removing the solvent, and crystallizing the product from methanol, there was obtained 7.85 g. (53%) of crystalline lactone, m. p. 112–113.5°. The recrystallized material formed granular prisms, m. p. 115–115.5°.

Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.16; H, 6.90. Found: C, 82.43; H, 6.96.

2-(6,α-Dimethyl-7-tetralylmethyl)-benzoic Acid.—The lactone III (8 g.) was refluxed for forty-two hours with amalgamated zinc (400 g.), toluene (150 cc.), glacial acetic acid (40 cc.), concentrated hydrochloric acid (160 cc.), and water (80 cc.), with three further additions of 50-cc. portions of acid. The product was extracted with benzene and the acidic portion taken into 10% sodium carbonate solution, precipitated, and dried in ether. Evaporation left a colorless oil which was obtained crystalline from methanol containing 10% of water; yield, 2.2 g., m. p. 165–165.5°. In a second reduction 5.5 g. of lactone gave 1.75 g. of the acid, and the combined neutral material from the two experiments on further reduction gave 0.9 g. of acid; total yield 13.5 g. (36%).

Recrystallized from aqueous methanol, the acid formed micro-needles, m. p. 165.5–166°; occasionally a second form was obtained melting at 147–148° and remelting after fusion at 165.5–166°.

Anal. Calcd. for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.63; H, 7.68.

1′,2′,3′,4′-Tetrahydro-4,10-dimethyl-1,2-benz-9-anthrone (IV).—The above acid (2.2 g.) was dissolved slowly in 50 cc. of concentrated sulfuric acid at room temperature and after one hour the red solution was poured onto ice and the precipitate extracted with ether. The ether solution, washed with water, soda and water, was dried and evaporated and the residue crystallized from methanol. This gave 1.6 g., m. p. 112–113°, and 0.18 g., m. p. 111–112°; yield, 86%. The recrystallized anthrone formed colorless blades, m. p. 112.8–113.4°.

Anal. Calcd. for $C_{20}H_{20}O$: C, 86.92; H, 7.30. Found: C, 87.41; H, 7.49.

1′,2′,3′,4′-Tetrahydro-4,10-dimethyl-1,2-benzanthracene (V). For reduction, 3 g. of IV in 10 cc. of toluene was refluxed for thirty hours with 5 g. of zinc dust and 75 cc. of 2 *N* sodium hydroxide, with the further addition of 10 g. of zinc and 100 cc. of alkali. In contrast to the behavior noted in the reduction of the anthrone VIII, no fluorescence developed in the course of the reaction, probably because the intermediate dihydroanthranol persists in the alkaline medium and escapes dehydration. The reaction mixture was extracted thoroughly with benzene, and on washing the extract with dilute hydrochloric acid it acquired a fluorescence which became more pronounced on concentrating the washed solution. After removing the solvent the residual oil was distilled at 2 mm., yielding a yellow, fluorescent distillate which formed crystals, m. p. 77–80° from methanol (2.02 g.). As the melting point was not improved by recrystallization, the product was dissolved in alcohol with 3 g. of picric acid, yielding 2 g. of violet-black picrate, m. p. 145–146°. This was decomposed with sodium carbonate solution–benzene, giving 1.05 g. (37%) of microcrystalline hydrocarbon, m. p. 104–105°. Recrystallized from methanol, the substance formed pale yellow micro-needles, m. p. 105–105.5°. The purified picrate formed slender, violet-black needles, m. p. 146–147°.

Anal. Calcd. for $C_{20}H_{20}$: C, 92.26; H, 7.74. Found: C, 91.87; H, 8.01.

4,10-Dimethyl-1,2-benzanthracene.—For dehydrogenation 540 mg. of the tetrahydride V was heated with 120 mg. of sulfur for four hours at 190–215° in an atmosphere of nitrogen. The material collected after extraction with benzene and purification by chromatographic adsorption proved to be a mixture and the separation of a satisfactory product was a tedious process which need not be described in detail but which involved selective adsorption on alumina (some tetrahydride passed into the filtrate and was treated again with sulfur), elution with benzene–methanol, and fractionation both as the picrate and as the hydrocarbon. The best sample of picrate formed long black needles, m. p. 161.5–162°. After collecting in all 235 mg. of picrate melting at 161.3–161.9°, decomposition with sodium carbonate solution yielded 79 mg. of hydrocarbon, m. p. 108.5–111.5°, and further recrystallizations from methanol gave 17.5 mg. (3%) of opaque, pale yellow needles melting at 114–114.4° (softening at 113°).

Anal. Calcd. for $C_{70}H_{16}$: C, 93.70; H, 6.30. Found: C, 93.54; H, 6.61.

Summary

6-Methyltetralin, prepared by the catalytic hydrogenation of β-methylnaphthalene, is substituted in the 7-position in the Friedel and Crafts reaction with phthalic anhydride. The resulting keto acid has been used as the starting material for the synthesis of the 4-methyl and the 4,9- and 4,10-dimethyl derivatives of 1,2-benzanthracene, as well as their 1′,2′,3′,4′-tetrahydro derivatives, all of which are of interest in investigating the relationship between structure and carcinogenic activity. Although the syntheses were completed successfully, some difficulty was experienced in the dehydrogenations, apparently because of the ease of elimination of meso alkyl groups.

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Separation of Sulfuric Acid from Nitric, Alkyl- and Arylsulfonic, and Alkylsulfuric Acids by Means of Liquid Ammonia

BY JOHN H. BILLMAN AND L. F. AUDRIETH

The ammonium salts of many oxy acids such as sulfuric, phosphoric, oxalic and arsenic are insoluble in liquid ammonia. Use has been made of the insolubility of some of these ammonium salts in liquid ammonia to effect the preparation of such nitrogen bases as hydrazine,[1] semicarbazide[2] and hydroxylamine[2] by ammonolysis of the respective sulfates, oxalates, phosphates and arsenates. The nitrogen bases are very soluble in liquid ammonia and are recovered in the anhydrous condition by evaporation of the solvent.

This marked insolubility of ammonium sulfate in liquid ammonia suggested that liquid ammonia might be used for the removal of excess sulfuric acid where the latter is employed either by itself or with other reagents. The experimental results reported in this paper demonstrate that it is possible (1) to separate quantitatively sulfuric and nitric acids by conversion into the ammonium salts and extraction of soluble ammonium nitrate with liquid ammonia; (2) to use liquid ammonia as a solvent for alkyl- and arylsulfonic acids, as well as alkylsulfuric acids; (3) to use liquid ammonia for the removal of excess sulfuric acid from compounds of the types listed under (2), especially where it is desired to produce directly the ammonium salts of the alkyl- and arylsulfonic acids and alkylsulfuric acids.

Experimental

It should be emphasized that no special apparatus is necessary in using liquid ammonia for the reactions outlined below. Filtration is carried out using ordinary Büchner funnels and filter flasks. It is a simple task to cool the funnel and flask quickly by running a small quantity of liquid ammonia through the filter. Filtration is simplified where sintered glass crucibles or filter funnels are used in place of filter paper. Naturally, good ventilation is not only desirable, but necessary.

Separation of Sulfuric Acid from Nitric Acid.—The separation and recovery of nitric and sulfuric acids in the spent acids after use in nitration reactions, by conversion into ammonium salts and extraction with liquid ammonia is practically quantitative. In a typical experiment a solution containing 20.8 g. of 96% sulfuric acid and an approximately equal quantity of concentrated nitric acid was neutralized with concentrated aqueous ammonia. The solution was evaporated and the solid residue treated with 200 cc. of liquid ammonia. The insoluble ammonium sulfate was removed by filtration, washed with liquid ammonia, heated at 60°[3] for several hours and weighed; yield, 26.8 g. of ammonium sulfate corresponding to a 99.3% recovery. No sulfate was found to be present in the ammonium nitrate recovered from the filtrate.

Solubility of Alkyl- and Arylsulfonic Acids and Alkylsulfuric Acids in Liquid Ammonia at −33°.—A representative number of compounds of this type were prepared and their solubility in liquid ammonia tested qualitatively. With the exception of laurylsulfuric acid, all compounds listed below are readily and easily soluble to the extent of at least 10 g. in 100 cc. of ammonia. Solution of these acids in liquid ammonia brings about their conversion into the ammonium salts. In a number of cases the products obtained upon evaporation of the liquid ammonia solution were recrystallized from absolute alcohol and analyzed for their nitrogen content. These compounds are listed in Table I.

In extending this study to other derivatives of these acids, it was found that the sodium salts of benzenesulfonic acid and *n*-butylsulfonic acid are very soluble in liquid ammonia, whereas the sodium salts of laurylsulfuric and benzylsulfonic acids are only slightly soluble.

(1) Browne and Welsh, THIS JOURNAL, **33**, 1728 (1911).
(2) Audrieth, *ibid.*, **52**, 1250 (1930).
(3) Heating is necessary due to the fact that ammonium sulfate forms a number of ammonates which must be decomposed to obtain the anammonous salt.