available to them, and to Mr. Vernon N. Kerr, also of LASL, for technical assistance. Financial support from the Industrial Hygiene Laboratory of Sandia Corporation, as well as encouragement from Mr. William H. Kingsley of that Laboratory, were also greatly appreciated.

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

The Synthesis of 2'-Fluoro-10-methyl-1,2-benzanthracene[1]

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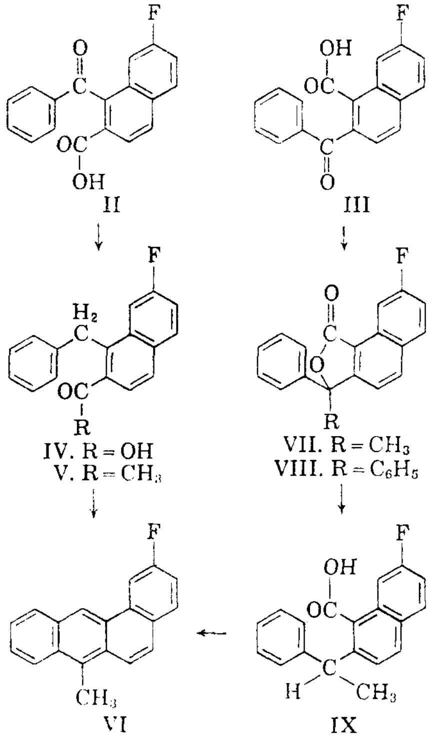
The Friedel-Crafts condensation of 7-fluoro-1,2-naphthalic anhydride, I, with benzene affords about equal amounts of 1-benzoyl-7-fluoro-2-naphthoic acid (II) and 2-benzoyl-7-fluoro-1-naphthoic acid (III). Each of these acids is converted into 2'-fluoro-10-methyl-1,2-benzanthracene (VI), as shown in the charts.

In continuation of a previously described program of synthesis designed to provide all of the monofluoro-10-methyl-1,2-benzanthracenes[2] for studies on carcinogenicity we have prepared 2'-fluoro-10-methyl-1,2-benzanthracene by the routes outlined in the chart.



The keto acids, II and III, were prepared by the Friedel-Crafts condensation of 7-fluoro-1,2-naphthalic anhydride (I) with benzene. Although this condensation was not studied in great detail, it was shown that the acids II and III were formed in about equal amounts, in addition to a small but variable amount (5–17% in different runs) of the phthalide VIII. Thus, the overall condensation at the unhindered carbonyl group of I was slightly greater than the condensation at the hindered carbonyl of I. This result may be compared with those in the condensation of benzene with 3-methylphthalic anhydride[3] (about equal amount of condensation at the hindered and unhindered carbonyls) and with 3-chlorophthalic anhydride[4] (condensation entirely at the hindered (2-position) carbonyl). The condensation of 1,2-naphthalic anhydride with benzene has been reported[5] but the relative amounts of the isomeric acids produced were not determined.

As the main objective of this research program was to provide 2'-fluoro-10-methyl-1,2-benzanthracene (VI) for biological experimentation,[2] a minimum of developmental work was done. Acid II was converted into VI in about 13% overall yield and III into VI in about 12% overall yield as shown in the chart.

EXPERIMENTAL[6]

β-(p-Fluorobenzoyl)propionic acid. To a stirred solution of 50 g. (0.5 mole) of succinic anhydride in 300 ml. of *o*-dichlorobenzene and 55 ml. (0.6 mole) of fluorobenzene[7] held at 50–60° was added gradually 134 g. (1.0 mole) of powdered anhydrous aluminum chloride. The reaction mixture was held

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[1] This research was supported by a Grant, C-4395, from the U.S. Public Health Service.

[2] M. S. Newman, D. MacDowell, and S. Swaminathan, *J. Org. Chem.*, **24**, 509 (1959). For a report on the biological activity of the fluorinated compounds prepared in this laboratory see H. A. Hartmann, E. C. Miller, and J. A. Miller, *Proceedings for Experimental Biology and Medicine*, **101**, 626 (1959), and E. C. Miller and J. A. Miller, *Cancer Research*, **20**, 133 (1960).

(3) M. S. Newman and C. D. McCleary, *J. Am. Chem. Soc.*, **63**, 1542 (1941).

(4) M. S. Newman and P. G. Scheurer, *J. Am. Chem. Soc.*, **78**, 5004 (1956).

(5) H. Waldmann, *J. prakt. Chem.*, **127**, 195 (1930); **131**, 71 (1931).

(6) All melting points of pure compounds are corrected. Microanalyses by Galbraith Microanalytical Laboratories, Knoxville, Tenn., and by Schwarzkopf Microanalytical Laboratories,

(7) We acknowledge with thanks a generous gift of fluorobenzene from the Penn Salt Chemicals Corp., Three Penn Center, Philadelphia 2, Pa.

at 50–60° for 5 hr. and at 70–80° for 2 hr. and was then poured on ice and hydrochloric acid. A conventional workup afforded 92 g. (94% based on succinic anhydride) of β-(p-fluorobenzoyl)propionic acid,[8] m.p. 100–102°, sufficiently pure for the next step. One recrystallization from aqueous methanol afforded pure acid, m.p. 102.5–103.5°.

γ-(p-fluorophenyl)butyric acid. Clemmensen-Martin reduction[9] of the above acid yielded γ-(p-fluorophenyl)butyric acid,[10] m.p. 38.5–39.5°, in 80% yield.

Anal. Calcd. for $C_{10}H_{11}FO_2$: C, 65.9; H, 6.0. Found: C, 66.1; H, 6.1.

The ethyl ester of the above acid, b.p. 124–127° at 8–9 mm. was prepared by acid-catalyzed esterification.

Anal. Calcd. for $C_{12}H_{15}FO_2$: C, 68.6; H, 7.1. Found: C, 68.9; H, 7.2.

7-Fluoro-1,2-naphthalic anhydride (I). As in the case of ethyl γ-phenylbutyrate,[11] the above ester was converted into 7-fluoro-3,4-dihydro-1,2-naphthalic anhydride, m.p. 127–128°, in 60% yield.

Anal. Calcd. for $C_{12}H_7FO_3$: C, 66.1; H, 3.2. Found: C, 66.1; H, 3.3.

Treatment of the dihydroanhydride with one equivalent of sulfur at 240–250° for about 20 min. and at 260–270° for 35 min. afforded crude I, m.p. 102–110°. This material was refluxed in benzene (10 ml./g.) containing freshly precipitated copper powder (4 g. product/1 g. Cu) for 7 hours. Filtration, concentration, dilution with petroleum ether (b.p. 60–69°), and crystallization afforded I, m.p. 143–145°, in 71% yield. Material of this purity was used in further work. The analytical sample melted at 148.5–149.5°.

Anal. Calcd. for $C_{12}H_5FO_3$: C, 66.7; H, 2.3; F, 8.8. Found: C, 66.7; H, 2.3; F, 8.9.

Condensation of I *with benzene.* To a stirred solution of 10.8 g. of I in 150 ml. of benzene was added in portions 16 g. of aluminum chloride. The mixture became deep red and was refluxed for 4 hr. After a conventional workup there was isolated 1.1 g. (6.2%) of crude VIII, m.p. 154–156°, (see below) and 12.6 g. (80%) of acid mixture, m.p. 152–160°, which was separated into its components by a procedure similar to that described[8] except that 4 ml. of 100% sulfuric acid was used per gram of mixed methyl esters and the resulting solution was held at 20–25° for 3 hr. Of the original acid mixture, m.p. 152–160°, there were obtained III, m.p. 174–178°, in 46% yield and II as the methyl ester, m.p. 118–121°. One crystallization of the latter from methanol afforded the pure methyl ester, m.p. 130–131°, in 42% yield.

The analytical sample of 2-benzoyl-7-fluoro-1-naphthoic acid, III, obtained with little loss on recrystallization from dilute ethanol, melted at 184.5–185.5°. The analytical sample of 1-benzoyl-7-fluoro-2-naphthoic acid, II, obtained by alkaline hydrolysis of the ester, melted at 211.0–212.0°.

Anal. Calcd. for $C_{18}H_{11}FO_3$: C, 73.5; H, 3.8. Found: C, 73.3; H, 3.7. (for III) C, 73.6; H, 3.8.

The analytical sample of methyl 1-benzoyl-7-fluoro-2-naphthoate melted at 131.2–132.2°.

Anal. Calcd. for $C_{19}H_{13}FO_3$: C, 74.0; H, 4.3. Found: C, 74.0; H, 4.3.

Proof of structure of II. After heating a solution of II in quinoline containing powdered copper bronze at 230–240° for 0.5 hr., the neutral portion yielded an oily ketone, purified by chromatography and characterized by its infrared absorption spectrum and its red 2,4-dinitrophenylhydrazone, m.p. 251–253°.

Anal. Calcd. for $C_{23}H_{15}FN_4O_4$: C, 64.2; H, 3.5; N, 13.0. Found: C, 64.0; H, 3.5; N, 13.0.

Authentic 1-benzoyl-7-fluoronaphthalene was prepared as follows. Part (42 g.) of the crude product obtained by condensation of ethyl oxalate with ethyl γ-(p-fluorophenyl)-butyrate (see above under preparation of I, ref. 11) was boiled with 350 ml. of 20% sulfuric acid for 18 hr. The crude acid was esterified. Distillation afforded 18 g. of crude ethyl δ-(p-fluorophenyl)-α-ketovalerate, b.p. 140–150° at 1 mm., which was heated at 85–90° with a 1:1 mixture (by volume) of polyphosphoric acid and methanesulfonic acid[12] for 0.5 hr. The oil obtained by pouring on ice was heated for a short time with aqueous alcoholic alkali. The acid obtained from this treatment was crystallized from aqueous alcohol to yield 6 g. (23%) of 3,4-dihydro-7-fluoro-1-naphthoic acid,[13] m.p. 182.0–183.0°.

Anal. Calcd. for $C_{11}H_9FO_2$: C, 68.7; H, 4.7; F, 9.9. Found: C, 68.4; H, 4.8; F, 10.0,

After heating 10 g. of the dihydronaphthoic acid with 2 g. of sulfur at 240° for 0.5 hr., distillation afforded a solid which on recrystallization from acetic acid yielded 6 g. (60%) of 7-fluoro-1-naphthoic acid, m.p. 242.0–243.0°.

Anal. Calcd. for $C_{11}H_7FO_2$: C, 69.5; H, 3.7; F, 10.0. Found: C, 69.2; H, 4.0; F, 9.7.

Condensation of the acid chloride of 7-fluoro-1-naphthoic acid with benzene using aluminum chloride (room temperature-4 hr.) yielded 1-benzoyl-7-fluoronaphthalene as an oil, b.p. 184–186° at 0.5 mm.

Anal. Calcd. for $C_{17}H_{11}FO$: C, 81.6; H, 4.4; F, 7.6. Found: C, 81.5; H, 4.5; F, 7.5.

The identity of this ketone with that obtained by decarboxylation of 1-benzoyl-7-fluoro-2-naphthoic acid (II) was established by quantitative infrared analysis in carbon tetrachloride solution. The 2,4-dinitrophenylhydrazones of the two samples proved unsatisfactory for comparison.

2′-Fluoro-10-methyl-1,2-benzanthracene (VI) (a) *Via* II. A mixture of 4.2 g. of II, 10 g. of potassium hydroxide, 12 g. of zinc dust (activated with copper sulfate), and 60 ml. of water was refluxed for 36 hr. Crystallization of the crude acid fraction from 80% ethanol yielded 2.6 g. of 1-benzyl-7-fluoro-2-naphthoic acid, IV, m.p. 172–175°, pure enough for further work. The analytical sample melted at 193–194° and was obtained with little loss from lower melting acid. Polymorphic forms appear to be present.

Anal. Calcd. for $C_{18}H_{13}FO_2$: C, 77.1; H, 4.7. Found: C, 77.0; H, 4.7.

A solution of 7.0 g. of IV, m.p. 172–175°, in 500 ml. of dry ether was added to the methyllithium prepared from 2.3 g. of lithium and 27 g. of methyl iodide in 100 ml. of ether. After standing at about 20° for 1 hr., the mixture was treated with water and the neutral fraction of the reaction products was stirred into 100 ml. of polyphosphoric acid.[14] The resulting solution was held at about 115° for 5 hr. and was then poured on ice and worked up in the usual way. Chromatography of the neutral fraction followed by recrystallization from benzene and petroleum ether (b.p. 60–69°) afforded 1.3 g. (20%) of pure VI, m.p. 103.5–104.5°, as colorless prisms.

Anal. Calcd. for $C_{19}H_{13}F$: C, 87.7; H, 5.0; F, 7.3. Found: C, 87.6; H, 5.0; F, 7.4.

(b) *Via* III. To a warm solution of 14.7 g. of III, m.p. 174–178°, in 500 ml. of ether-benzene (1:1) was added the Grignard reagent prepared from 3.2 g. of magnesium and 17 g. of methyl iodide in 175 ml. of ether. After refluxing for 6 hr. the mixture was decomposed with dilute acid and separated as usual into acid (6.2 g., 42% of III, m.p. 166–170°) and neutral (8.5 g., 58% of VII, m.p. 178–182°) fractions.

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(8) L. F. Fieser, M. T. Leffler, *et al.*, *J. Am. Chem. Soc.*, **70**, 3197 (1948).

(9) E. L. Martin, *J. Am. Chem. Soc.*, **58**, 1438 (1936).

(10) Ref. 8 above states that this acid "melts about 30°."

(11) L. F. Fieser and E. B. Hershberg, *J. Am. Chem. Soc.*, **57**, 1851 (1935).

(12) We acknowledge with thanks a generous gift of methanesulfonic acid from the Standard Oil Company of Indiana through the courtesy of Drs. B. Shoemaker and T. Tom.

(13) Compare procedure in M. S. Newman and K. Rutherford, *J. Am. Chem. Soc.*, **79**, 213 (1957).

(14) We are indebted to the Victor Chemical Works, Chicago, Ill., for a generous gift of polyphosphoric acid.

Recrystallization of part of the latter yielded pure lactone of 2-(α-hydroxy-α-methylbenzyl)-7-fluoro-1-naphthoic acid, VII, m.p. 193.0–194.0°.

Anal. Calcd. for $C_{19}H_{13}FO_2$: C, 78.0; H, 4.5. Found: C, 77.7; H, 4.8.

Hydrogenation of 4.0 g. of VII, m.p. 178–182° in alcohol in the presence of 0.4 g. of palladium chloride and 4.0 g. of charcoal (Darco G-60) for 18 hr. at 40 p.s.i. and at 20° gave 3.0 g. (75%) of pure 2-(α-methylbenzyl)-7-fluoro-1-naphthoic acid (IX), m.p. 172.0–173.0°, on recrystallization from aqueous-ethanol.[15]

Anal. Calcd. for $C_{19}H_{15}FO_2$: C, 77.6; H, 5.1. Found: C, 77.5; H, 5.3.

When 1.0, g. of IX, m.p. 165–168°, was treated as described[16] VI, m.p. 102.0–103.0°, was obtained in 40% yield after purification as above. A mixed m.p. with the sample of VI prepared from II showed no depression.

Lactone of 2-(α-hydroxy-α-phenylbenzyl)-7-fluoro-1-naphthoic acid (VIII). To a Grignard reagent prepared from 1 g. of magnesium and 6.3 g. of bromobenzene in 50 ml. of ether was added a solution of 5.9 g. of III, m.p. 174–178°, in 100 ml. of benzene. After refluxing for 16 hr. the reaction mixture yielded 4.2 g. (60%) of VIII, m.p. 156–158°. Recrystallization from benzene-petroleum ether (b.p. 60–69°) afforded the analytical sample, m.p. 163.0–164.0°, which was not depressed by mixing with a sample of VIII obtained (see above) from the condensation of I with benzene.

Anal. Calcd. for $C_{24}H_{15}FO_2$: C, 81.4; H, 4.2. Found: C, 81.7; H, 4.3.

In addition to mixed melting point determinations, the identity of samples of supposedly identical compounds was checked by infrared analysis.

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(15) Catalytic hydrogenation was found to be superior to zinc and acid[9] or zinc and alkali reductions. The latter methods gave poor yields of reduced acid and considerable starting material was recovered unchanged. See forthcoming publication of M. S. Newman and E. H. Wiseman for further discussion.

(16) Compare to conversion of compound VIII to X in L. F. Fieser and M. S. Newman, *J. Am. Chem. Soc.*, **58**, 2376 (1936).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE VIRGINIA POLYTECHNIC INSTITUTE]

Some New 9-Dimethylphenylanthracenes

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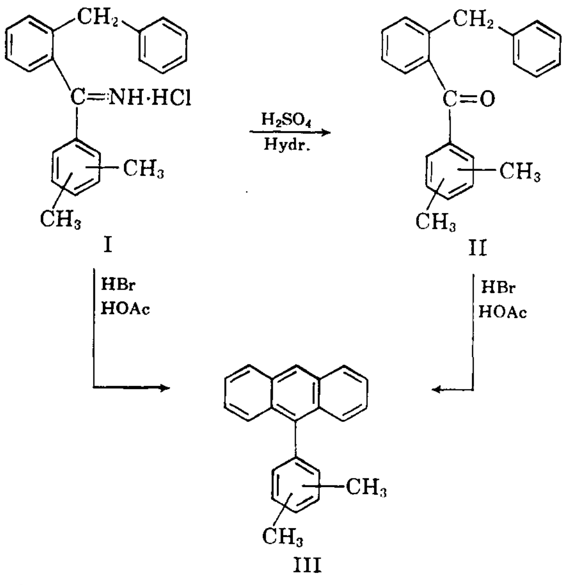
Using previously described methods of cyclization, a series of new 9-dimethylphenylanthracenes has been prepared. Six new ketimine hydrochlorides and six new ketones which are intermediates in the syntheses were isolated. Three additional new ketimine hydrochlorides were also prepared to complete previously reported work.

Bradsher's method of aromatic cyclodehydration[2] for the preparation of hydrocarbons was introduced in 1940. Later publications extended the usefulness of this synthesis. So for example, Bradsher and Vingiello[3] prepared a series of 9-(monosubstituted phenyl)anthracenes and Vingiello and Bořkovec[4] prepared a series of 9- and 10-(monosubstituted phenyl)-1,2-benzanthracenes. We have now extended Bradsher's aromatic cyclodehydration reaction to the preparation of 9-dimethylphenylanthracenes.

The reaction between 2-cyanodiphenylmethane and the appropriate Grignard reagent led to good yields of the ketimines, isolated as the hydrochlorides I. Although these compounds could be prepared in good yields in a fair state of purity, the preparation of analytical samples proved quite difficult. This was due in part to the tendency of the compounds (I) to hydrolyze and in part to the fact that the compounds melted with decomposition over a wide temperature range. Of the six possible isomers, the 3,4- and 3,5-dimethyl compounds (I, 3,4- and 3,5-dimethyl) were found to hydrolyze most readily and the 2,6-dimethyl compound (I, 2,6-dimethyl) was found to hydrolyze only with great difficulty.[5]



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(1) This paper has been abstracted in part from the Master's thesis of Edward Kramer and the Doctorate thesis of Sih-gwan Quo presented to the Virginia Polytechnic Institute in 1954 and 1959 respectively.

(2) C. K. Bradsher, *J. Am. Chem. Soc.*, **62**, 486 (1940).

(3) C. K. Bradsher and F. A. Vingiello, *J. Am. Chem, Soc.*, **71**, 1434 (1949).

(4) F. A. Vingiello and A. Bořkovec, *J. Am. Chem. Soc.*, **77**, 4823 (1955) and references listed there.

(5) J. B. Culbertson's results in a study of the factors affecting the rates of hydrolysis of substituted diphenylketimines, *J. Am. Chem. Soc.*, **73**, 4818 (1951), clearly imply that the difficulty is due to steric hindrance.