Substituent Effects. VIII.[1] Synthesis of Substituted α- and β-Fluoronaphthalenes[2]

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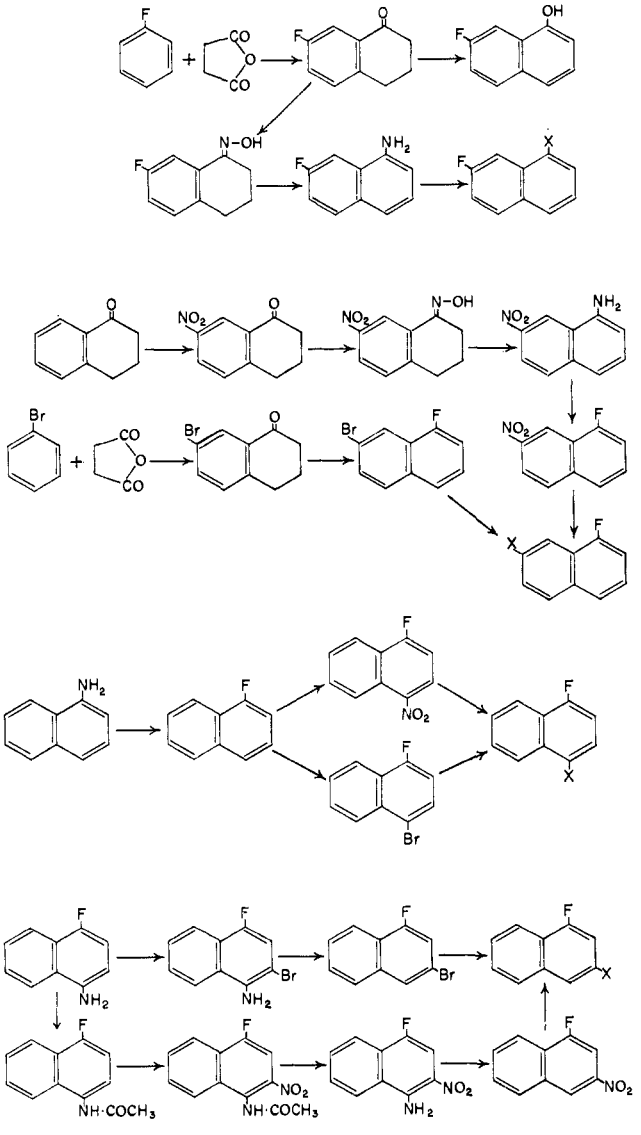
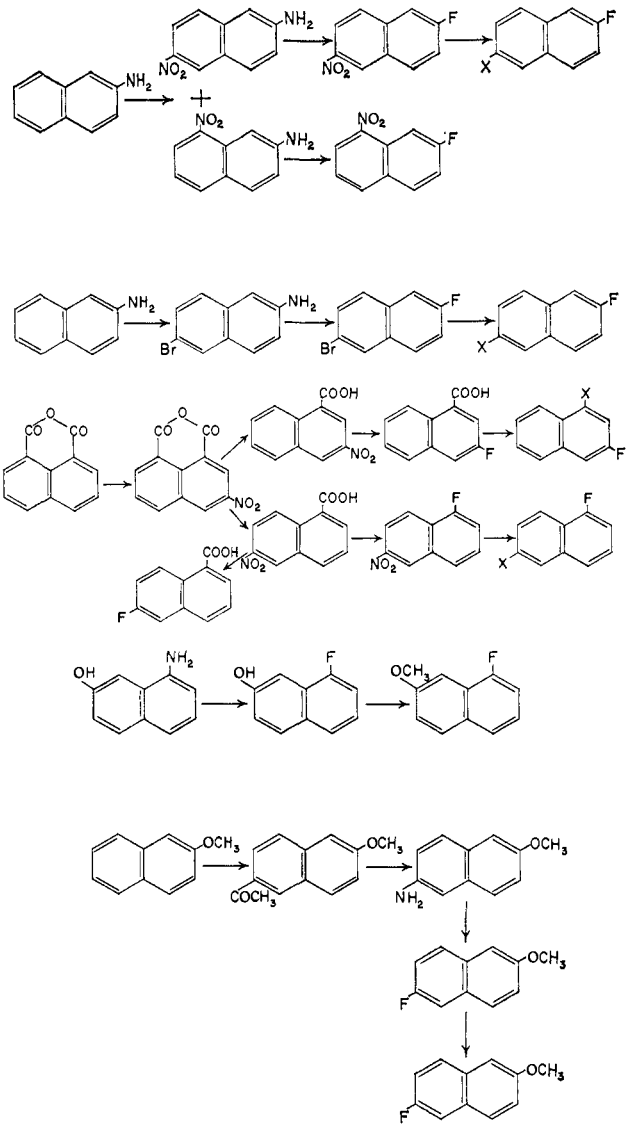
Abstract: This paper describes the synthesis and characterization of 55 derivatives of α- and β-fluoronaphthalene which were required for the studies of substituent effects reported in part VII.

For reasons indicated in the preceding paper of this series, we needed a range of derivatives of α- and β-fluoronaphthalene-carrying substituents in as many as possible of the unhindered positions (*i.e.*, positions neither *ortho* nor *peri* to fluorine) and with unambiguous orientation. This paper describes the synthesis of 55 compounds of this type, most of which were previously unknown, by the routes indicated in the following charts.





Experimental Section

Unless otherwise stated, the conversion of amines to fluoro compounds *via* the corresponding diazonium hexafluorophosphates followed the procedure used for 6-fluoro-2-nitronaphthalene. Melting points are uncorrected.

2-Nitro-6-fluoronaphthalene. 2-Amino-6-nitronaphthalene[1] (10 g) was diazotized according to the procedure of Adock and Wells.[3] After 15 min, the light pinkish brown diazonium hexafluorophosphate salt was precipitated by rapid addition of 65% hexafluorophosphoric acid (23 ml). The salt (18 g) was collected and dried *in vacuo*, mp 125–126° dec.

(1) Part VII: W. Adcock and M. J. S. Dewar, *J. Am. Chem. Soc.*, **89**, 379 (1967).

(2) This work was supported by the Army Research Office through Grant No. DA-ARO-D-31-124-G713.

(3) W. Adcock and P. R. Wells, *Australian J. Chem.*, **18**, 1351 (1965).

The dry powdered solid was decomposed in hot (130–140°) mineral oil in the usual manner,[4] and the 2-fluoro-6-nitronaphthalene (4.4 g) was recovered by basification (Na_2CO_3) and steam distillation. After recrystallization twice from *n*-hexane it formed pale yellow needles, mp 109.5–110.5°.

Anal. Calcd for $C_{10}H_6O_2NF$: C, 62.83; H, 3.16; N, 7.33. Found: C, 63.03; H, 3.23; N, 7.32.

2-Amino-6-fluoronaphthalene. A solution of 2-fluoro-6-nitronaphthalene (6 g) in ethanol (200 ml) was reduced with hydrogen (50 psi) over palladized charcoal (5%). After 3 hr the solution was filtered and evaporated *in vacuo*, and the amine hydrochloride precipitated from a solution of the residue in dry ether with hydrogen chloride. The free amine, liberated from the salt by sodium carbonate, crystallized from Skellysolve B in light pink plates (3 g), mp 110–111°.

Anal. Calcd for $C_{10}H_8NF$: C, 74.52; H, 5.00; N, 8.69. Found: C, 74.73; H, 5.11; N, 8.80.

2-Acetamido-6-fluoronaphthalene. A solution of 2-amino-6-fluoronaphthalene (1 g) in glacial acetic acid (20 ml) and acetic anhydride (0.6 g) was warmed on a steam bath for 30 min and then evaporated *in vacuo*. The acetyl derivative, after crystallization twice from aqueous ethanol (Norit), and then from Skellysolve B–ethyl acetate (2:1), formed colorless plates, mp 146–147°.

Anal. Calcd for $C_{12}H_{10}ONF$: C, 70.92; H, 4.96; N, 6.89. Found: C, 71.00; H, 5.04; N, 7.05.

2-Fluoro-6-bromonaphthalene. 2-Amino-6-bromonaphthalene[3] was diazotized, and the yellow diazonium hexafluorophosphate (35 g) precipitated with 65% hexafluorophosphoric acid (30 ml), mp 115–118° dec (lit.[5] 107–110° dec). Decomposition of the salt in mineral oil at 130–140°, followed by steam distillation and crystallization from *n*-hexane, gave white glistening plates of 2-bromo-6-fluoronaphthalene, mp 64.5–65.5° (lit.[5] mp 66–67°).

Anal. Calcd for $C_{10}H_6FBr$: C, 53.37; H, 2.69. Found: C, 53.60; H, 2.81.

2-Cyano-6-fluoronaphthalene. A solution of 2-bromo-6-fluoronaphthalene (11 g, 0.049 mole), cuprous cyanide (4.48 g, 0.05 mole), dimethylformamide (50 ml), and four drops of pyridine was heated under reflux for 5 hr. The product was worked up according to Dewar and Grisdale[6] and after three recrystallizations (with one Norit decolorization) from Skellysolve B gave white fluffy needles of 6-fluoro-2-cyanonaphthalene (4 g), mp 130.5–131.5°.

Anal. Calcd for $C_{11}H_6NF$: C, 77.18; H, 3.53; N, 8.18. Found: C, 76.97; H, 3.47; N, 8.15.

6-Fluoro-2-naphthoic Acid. A mixture of 2-cyano-6-fluoronaphthalene (2 g), glacial acetic acid (30 ml), concentrated sulfuric acid (15 ml), and water (15 ml) was heated under reflux for 14 hr and cooled. The precipitate was treated with 10% sodium carbonate solution and filtered; the filtrate was acidified with dilute hydrochloric acid, yielding crude 6-fluoro-2-naphthoic acid (2 g), which after recrystallization from aqueous ethanol formed white needles, mp 242–243.5° (lit.[3] mp 238–240°).

Anal. Calcd for $C_{11}H_7O_2F$: C, 69.47; H, 3.68. Found: C, 69.42; H, 3.61.

Methyl 6-Fluoro-2-naphthoate. Prepared from the fluoro acid and diazomethane in dioxane, the ester was recrystallized from Skellysolve B in white plates, mp 82–82.5° (lit.[3] 82–82.5°).

2-Methoxy-6-fluoronaphthalene. 2-Acetyl-6-methoxynaphthalene, prepared according to Robinson and Rydon,[7a] crystallized from methanol in white plates, mp 104–106° (lit.[7a] 104–105°). Schmidt rearrangement[7b] of the ketone (40 g), with hydrazoic acid in chloroform and concentrated sulfuric acid, first at 0°, and then at room temperature, gave 2-acetamido-6-methoxynaphthalene which was hydrolyzed by heating with ethanol (700 ml) and concentrated sulfuric acid (70 ml) on a steam bath for 1 hr. The hot alcoholic solution was poured onto ice, and the amine, isolated *via* its sulfate, had mp 146–148° (lit.[8] 139–140°).

Anal. Calcd: mol wt, 173. Found: mol wt (mass spectroscopy), 173.

The dry powdered amine sulfate (28 g) was diazotized by adding a solution of sodium nitrite (9 g) in water (20 ml) to a suspension in sulfuric acid (200 ml of 2 *N*) below 0°. The pale yellow diazonium hexafluorophosphate (37 g, mp 109–111° dec) was precipitated in the usual manner and decomposed in mineral oil at 130°; the product was steam distilled, giving crude 2-methoxy-6-fluoronaphthalene (7 g), which crystallized from Skellysolve B in white plates, mp 59.5–60.5°.

Anal. Calcd for $C_{11}H_9OF$: C, 75.00; H, 5.15; mol wt, 176. Found: C, 75.15; H, 5.32; mol wt (mass spectroscopy), 176.

6-Fluoro-2-naphthol. A suspension of crude 2-methoxy-6-fluoronaphthalene (5 g) in glacial acetic acid (25 ml) and 48% hydrobromic acid (150 ml) was refluxed for 2 hr and then poured onto ice. The precipitate was collected, dried, and recrystallized from Skellysolve B giving 6-fluoro-2-naphthol as white plates, mp 116–117.5°.

Anal. Calcd for $C_{10}H_7OF$: C, 74.06; H, 4.35; mol wt, 162.2. Found: C, 73.88; H, 4.47; mol wt (mass spectroscopy), 162.

β-(*p*-Fluorobenzoyl)propionic Acid. Finely powdered succinic anhydride (50 g, 0.5 mole) and powdered aluminum chloride (135 g, 1.0 mole) were thoroughly mixed in a 2-l., wide-mouthed flask, and fluorobenzene (163 g, 1.7 moles) was added all at once. After the initial vigorous evolution of hydrogen chloride had subsided, the solution was warmed on a steam bath for 1 hr, then cooled, and ice and concentrated hydrochloric acid (135 ml) were added. Excess fluorobenzene was steam distilled, leaving a residue which crystallized on standing. The crystals were dissolved in sodium carbonate and again steam distilled; acidification gave β-(*p*-fluorobenzoyl)propionic acid (61 g), which after recrystallization from aqueous ethanol and then ethanol had mp 101–102.5°.

Anal. Calcd for $C_{10}H_9O_3F$: C, 61.25; H, 4.62. Found: C, 61.08; H, 4.58.

The structure of this compound was confirmed by oxidation with alkaline permanganate to *p*-fluorobenzoic acid, mp 184–186° (lit.[9] 182°, 184–186°).

γ-(*p*-Fluorophenyl)butyric Acid. Clemmensen reduction[10] of the crude keto acid (60 g) gave γ-(*p*-fluorophenyl)butyric acid as an oil (42 g), bp 115–116° (0.1 mm), which soldified; a sample after recrystallization, first from Skellysolve B and then from ether–petroleum ether, formed white plates, mp 45.5–46.5°.

Anal. Calcd for $C_{10}H_{10}O_2F$: C, 65.92; H, 6.09. Found: C, 65.76; H, 6.13.

7-Fluoro-1-tetralone. γ-(*p*-Fluorophenyl)butyric acid was converted to the acid chloride, bp 103–105° (5 mm), with thionyl chloride. The acid chloride (37.1 g) was cyclized[11] to 7-fluoro-1-tetralone, which crystallized from petroleum ether–ether and then Skellysolve B, in long colorless needles (29 g), mp 63.5–65.0°.

Anal. Calcd for $C_{10}H_9OF$: C, 73.16; H, 5.53. Found: C, 73.34; H, 5.38.

7-Fluoro-1-tetralone Oxime. Prepared by refluxing a mixture of the fluorotetralone (45 g, 0.27 mole), ethanol (600 ml), pyridine (300 ml), and hydroxylamine hydrochloride (38.23 g, 0.55 mole) for 3 hr, the oxime crystallized from aqueous ethanol in white needles, mp 92–94°, raised by recrystallization from petroleum ether–ethyl acetate (3:1) to 92–93.5°.

Anal. Calcd for $C_{10}H_{10}ONF$: C, 67.03; H, 5.63; N, 7.82. Found: C, 66.81; H, 5.71; N, 7.90.

1-Amino-7-fluoronaphthalene. A solution of the oxime (30 g) in glacial acetic acid (100 ml) and acetic anhydride (20 ml) was saturated with dry hydrogen chloride and heated 30 min on a steam bath. The resulting 1-amino-7-fluoronaphthalene hydrochloride was collected, washed with ether, and then converted with ammonium hydroxide to 1-amino-7-fluoronaphthalene (13 g), which distilled at 110–115° (1 mm) as a colorless oil which solidified on standing, mp 36–38°.

Anal. Calcd for $C_{10}H_8NF$: C, 74.52; H, 5.00; N, 8.69. Found: C, 74.74; H, 5.05; N, 8.44.

An attempt to prepare this amine by aromatization of the azine of 7-fluoro-1-tetralone, using palladium–charcoal in triethylbenzene, gave a small amount of impure 1-amino-7-fluoronaphthalene. The azine crystallized from petroleum ether–ethyl acetate (2:1) in bright yellow needles, mp 143–145°.

Anal. Calcd for $C_{20}H_{18}N_2F_2$: C, 74.06; H, 5.59; N, 8.64. Found: C, 73.91; H, 5.63; N, 8.61.

1-Acetamide-7-fluoronaphthalene. This compound, obtained as a by-product when the aromatization of 7-fluoro-1-tetralone oxime (30 g) was carried out in a larger volume (500 ml) of glacial acetic

(4) K. G. Rutherford and W. Redmond, *Org. Syn.*, **43**, 12 (1963).
(5) M. S. Newman and R. H. B. Galt, *J. Org. Chem.*, **25**, 214 (1960).
(6) M. J. S. Dewar and P. J. Grisdale, *J. Am. Chem. Soc.*, **84**, 3539 (1962).
(7) (a) R. Robinson and H. N. Rydon, *J. Chem. Soc.*, 1399 (1993); (b) H. Wolff, *Org. Reactions*, **3**, 327 (1940).
(8) A. Windaus, *Ber.*, **57**, 1731 (1924).
(9) I. Heilbron and H. M. Bunbury, "Dictionary of Organic Compounds," Eyre and Spottiswoode, London, 1953.
(10) E. L. Martin, *J. Am. Chem. Soc.*, **58**, 1440 (1936).
(11) L. F. Fieser and A. M. Seligman, *ibid.*, **60**, 170 (1938).

acid, separated from aqueous ethanol in white needles, mp 163–164°.

Anal. Calcd for $C_{12}H_{10}ONF$: C, 70.92; H, 4.96; N, 6.89. Found: C, 71.08; H, 5.02; N, 7.07.

1-Dimethylamino-7-fluoronaphthalene. A suspension of 1-amino-7-fluoronaphthalene (7.8 g, 0.05 mole) and anhydrous sodium carbonate (15 g) in methyl iodide (25 g) and acetone (50 ml) was refluxed for 4 days, then filtered, and evaporated, and the residue extracted with ether. Removal of the ether gave an oil which was boiled with acetic anhydride (50 ml) for 24 hr, then evaporated, and the residue steam distilled, giving 1-dimethylamino-7-fluoronaphthalene (5.5 g), bp 114–115° (2 mm), $n^{26}D$ 1.5886.

Anal. Calcd for $C_{12}H_{12}NF$: C, 76.16; H, 6.39; N, 7.40. Found: C, 76.04; H, 6.36; N, 7.43.

1-Bromo-7-fluoronaphthalene. 1-Amino-7-fluoronaphthalene (3.5 g) was diazotized and added carefully to a solution of 48% hydrobromic acid (150 ml) and cuprous bromide (12 g) at 60°. The solution was then heated 1 hr, on a steam bath, cooled, and basified with a 10% sodium carbonate solution. Steam distillation gave crude 1-bromo-7-fluoronaphthalene (2.0 g) which distilled at 82–87° (0.8 mm) as an oil which solidified on cooling and after recrystallization from Skellysolve B formed needles, mp 43–44°.

Anal. Calcd for $C_{10}H_6BrF$: C, 53.37; H, 2.69. Found: C, 53.50; H, 2.84.

1-Cyano-7-fluoronaphthalene. 1-Amino-7-fluoronaphthalene (13.4 g) was diazotized, and the resulting solution was added carefully to a stirred solution of nickel chloride (36 g), potassium cyanide (41 g), and sodium hydroxide (11.5 g), in water (500 ml) at 0°. After 1 hr the solution was steam distilled, giving 1-cyano-7-fluoronaphthalene (11 g) which separated from Skellysolve B as a white microcrystalline solid, mp 93.5–94.5°.

Anal. Calcd for $C_{11}H_6NF$: C, 77.18; H, 3.53; N, 8.18. Found: C, 77.41; H, 3.59; N, 8.34.

7-Fluoro-1-naphthoic Acid. 1-Cyano-7-fluoronaphthalene was hydrolyzed using the procedure used to make 6-fluoro-2-naphthoic acid. The resulting 7-fluoro-1-naphthoic acid separated from aqueous ethanol in small white needles, mp 245.5–247.5°.

Anal. Calcd for $C_{11}H_7O_2F$: C, 69.47; H, 3.68. Found: C, 69.43; H, 3.82.

Methyl 7-Fluoro-1-naphthoate. Prepared from the fluoro acid by refluxing with methanol in the presence of sulfuric acid, the ester distilled at 108–109° (0.5 mm), $n^{26}D$ 1.5840.

Anal. Calcd for $C_{12}H_9O_2F$: C, 70.58; H, 4.44. Found: C, 70.45; H, 4.41.

7-Fluoro-1-naphthol. A suspension of 7-fluoro-1-tetralone (6 g) and 5% palladized charcoal (2.2 g) in triglyme (50 ml) was refluxed for 2 hr, then filtered into ice water, and extracted with ethyl acetate. Extraction with Claisen solution and neutralization with hydrochloric acid gave 7-fluoro-1-naphthol which crystallized from petroleum ether (Norit) in white needles, mp 138–139.5°.

Anal. Calcd for $C_{10}H_7OF$: C, 74.07; H, 4.32. Found: C, 74.30; H, 4.52.

1-Methoxy-7-fluoronaphthalene. A small excess of dimethyl sulfate was added to a solution of 7-fluoro-1-naphthol (1.6 g) in sodium hydroxide (0.59 g), and the mixture was warmed on a steam bath for 30 min. Excess dimethyl sulfate was destroyed with base, and the 1-methoxy-7-fluoronaphthalene was then isolated with ether as a colorless oil, bp 89–90° (1 mm), $n^{26}D$ 1.5880.

Anal. Calcd for $C_{11}H_9OF$: C, 75.00; H, 5.11. Found: C, 74.94; H, 5.22.

1-Fluoro-1-nitronaphthalene. A suspension of 1-amino-7-nitronaphthalene[12] hydrochloride (10 g) in concentrated hydrochloric acid (18 ml), water (28 ml), and ice (8 g) was diazotized by rapid addition of sodium nitrite (4 g) in water (20 ml) at 0°. After 10 min ice water (20 ml) was added, and the solution was filtered and treated with excess 65% hexafluorophosphoric acid giving the diazonium hexafluorophosphate, mp 138–139° dec, which was decomposed in the usual way to 1-fluoro-7-nitronaphthalene (4 g), pale yellow needles from Skellysolve B, mp 83.5–84.5°.

Anal. Calcd for $C_{10}H_{10}O_2NF$: C, 62.83; H, 3.16; F, 9.94; mol wt, 191. Found: C, 62.92; H, 3.36; F, 10.02; mol wt (mass spectroscopy), 191.

2-Amino-8-fluoronaphthalene. Prepared from the corresponding nitro compound in the same way as 2-amino-6-fluoronaphthalene, the amine crystallized from Skellysolve B (Norit) in pink plates, mp 53–54.5°.

(12) E. Berliner and E. W. Winicov, *J. Am. Chem. Soc.*, **81**, 1630 (1959).

Anal. Calcd for $C_{10}H_8NF$: C, 74.52; H, 5.00; N, 8.69. Found: C, 74.45; H, 5.20; N, 8.81.

2-Acetamido-8-fluoronaphthalene. Prepared from the above amine in the same way as the 2,6 isomer, the acetyl derivative crystallized from aqueous ethanol, then light petroleum ether–ethyl acetate, in white needles, mp 150.5–151.5°.

Anal. Calcd for $C_{12}H_{10}ONF$: C, 70.92; H, 4.96; N, 6.89. Found: C, 71.12; H, 5.16; N, 7.02.

2-Bromo-8-fluoronaphthalene. 7-Bromo-1-tetralone[11] oxime crystallized from aqueous ethanol in needles, mp 116–118° (lit.[13] 121°). Aromatization of the oxime (41 g) in acetic acid (300 ml) and acetic anhydride (20 ml) saturated with hydrogen chloride gave 1-amino-7-bromonaphthalene hydrochloride (15 g), mp 257–260° dec (lit.[14] 255° dec). The amine hydrochloride (15 g) was converted as above to the diazonium hexafluorophosphate, mp 135–137° dec, which on decomposition and steam distillation gave 2-bromo-7-fluoronaphthalene as a colorless oil, bp 86–88° (0.4 mm), $n^{26}D$ 1.5914, which was homogeneous to glpc.

Anal. Calcd for $C_{10}H_6FBr$: mol wt, 225. Found: mol wt (mass spectroscopy), 224, 226.

2-Cyano-8-fluoronaphthalene. Prepared from 1-bromo-7-fluoronaphthalene in the same way as the 2,6 isomer, 2-cyano-8-fluoronaphthalene crystallized from Skellysolve B in needles, mp 51–52.5°.

Anal. Calcd for $C_{11}H_6NF$: C, 77.18; H, 3.53; N, 8.18. Found: C, 77.31; H, 3.71; N, 7.98.

8-Fluoro-2-naphthoic Acid. Hydrolysis of the nitrile gave 8-fluoro-2-naphthoic acid, mp 242–243° (lit.[15] mp 241–242.5°).

Methyl 8-Fluoro-2-naphthoate. Prepared from the fluoro acid with diazomethane in dioxane, the ester crystallized from Skellysolve B in small white needles, mp 38.5–39°.

Anal. Calcd for $C_{12}H_9O_2F$: C, 70.58; H, 4.44. Found: C, 70.64; H, 4.51.

8-Fluoro-2-naphthol. Diazotization of 8-amino-2-naphthol gave a dark yellow-green solution which on filtration gave a tarry residue and a clear orange filtrate. Addition of excess 65% hexafluorophosphoric acid to the filtrate gave a small amount of the diazonium hexafluorophosphate, mp 120–124° dec, which was decomposed in hot (170°) mineral oil in the usual manner. The crude product was steam distilled, and the distillate was saturated with sodium chloride and extracted with ether. The fluoronaphthol was extracted from the ether solution with dilute potassium hydroxide and precipitated with carbon dioxide, forming a gray microcrystalline solid (1.15 g, 25%), mp 67–69.5°, raised by sublimation and crystallization from Skellysolve B to 96–97.5°.

Anal. Calcd for $C_{10}H_7OF$: C, 74.06; H, 4.35; F, 11.72. Found: C, 73.89; H, 4.25; F, 11.91.

2-Methoxy-8-fluoronaphthalene. Crude 8-fluoro-2-naphthol was methylated in the same way as the 7,1 isomer; the ether was distilled as a colorless oil, bp 84–86° (0.4 mm), $n^{26}D$ 1.5918.

Anal. Calcd for $C_{11}H_9OF$: C, 75.00; H, 5.15; mol wt, 176. Found: C, 74.81; H, 5.18; mol wt (mass spectroscopy), 176.

1-Nitro-4-fluoronaphthalene. 1-Fluoronaphthalene was nitrated in acetic acid by the method of Schiemann, *et al.*,[16] forming lachrymatory yellow needles, mp 75.5–77° (lit.[16] 80°).

1-Amino-4-fluoronaphthalene. Prepared from the above nitro compound in the same way as the 2,6 isomer, the amine distilled at 115–120° (1 mm) as a pale yellow oil which quickly solidified, mp 43–45° (lit.[16] 47°).

Anal. Calcd for $C_{10}H_8NF$: mol wt, 161. Found: mol wt (mass spectroscopy), 161.

1-Acetamido-4-fluoronaphthalene. The acetyl derivative separated from aqueous ethanol in white needles, mp 182–183°.

Anal. Calcd for $C_{12}H_{10}ONF$: C, 70.92; H, 4.96; N, 6.89; mol wt, 203. Found: C, 70.72; H, 4.89; N, 7.01; mol wt (mass spectroscopy), 203.

1-Dimethylamino-4-fluoronaphthalene. Prepared from 1-amino-4-fluoronaphthalene in the same way as the 1,7 isomer, the amine formed a pale yellow oil, bp 96–98° (1 mm), $n^{25}D$ 1.5965, which was homogeneous to glpc.

Anal. Calcd for $C_{12}H_{12}NF$: mol wt, 189. Found: mol wt (mass spectroscopy), 189.

(13) G. Schroeter, *Ber.*, **63**, 1285, 1292 (1930).
(14) K. Dziewonski and L. Sternbach, *Bull. Intern. Acad. Polon. Ser. A*, 59 (1931).
(15) M. J. S. Dewar and P. J. Grisdale, *J. Am. Chem. Soc.*, **84**, 3541 (1962).
(16) G. Schiemann, W. Gueffray, and W. Winkelmuller, *Ann.*, **487**, 270 (1931).

1-Fluoro-4-bromonaphthalene. 1-Fluoronaphthalene was brominated,[16] and the crude product was crystallized from petroleum ether, mp 35–36° (lit.[16] 37°).

1-Cyano-4-fluoronaphthalene. Prepared from the above bromo compound in the usual manner, the nitrile separated from Skellysolve B in needles, mp 89.5–90.5°.

Anal. Calcd for $C_{11}H_6NF$: C, 77.18; H, 3.53; N, 8.18; mol wt, 171. Found: C, 77.36; H, 3.57; N, 8.04; mol wt (mass spectroscopy), 171.

4-Fluoro-1-naphthoic Acid. Prepared by hydrolysis of the nitrile, the acid crystallized from aqueous ethanol in needles, mp 224–225°.

Anal. Calcd for $C_{11}H_7O_2F$: C, 69.47; H, 3.68. Found: C, 69.47; H, 3.72.

Methyl 4-Fluoro-1-naphthoate. Prepared from the fluoro acid by refluxing with methanol in the presence of sulfuric acid, the ester crystallized from Skellysolve B in plates, mp 52–53°.

Anal. Calcd for $C_{12}H_9O_2F$: C, 70.58; H, 4.44. Found: C, 70.74; H, 4.60.

1-Acetamido-2-nitro-4-fluoronaphthalene. Nitration of 1-acetamido-4-fluoronaphthalene (25 g) by the method of Hodgson and Birtwell[17] gave 1-acetamido-2-nitro-4-fluoronaphthalene (8 g) as golden needles (from ethanol), mp 227.5–229°.

Anal. Calcd for $C_{12}H_9N_2O_3F$: mol wt, 248. Found: mol wt (mass spectroscopy), 248.

The orientation followed from analogy[17] and from the deep color of the nitro compound.

1-Fluoro-3-nitronaphthalene. Hydrolysis of the acetyl derivative with alcoholic hydrochloric acid gave the orange amine, mp 168–170°, a solution of which (6.5 g) in glacial acetic acid (200 ml) was added dropwise to one of sodium nitrite (3.5 g) in concentrated sulfuric acid (25 ml) kept below 15°. After 1 hr, the diazonium solution was added carefullly to a suspension of cuprous oxide (50 g) in ethanol (600 ml). Evaporation and steam distillation gave 2-nitro-4-fluoronaphthalene (3 g) as yellow needles (from ethanol), mp 93–94°.

Anal. Calcd for $C_{10}H_6NO_2F$: C, 62.83; H, 3.16; N, 7.33; mol wt, 191. Found: C, 62.97; H, 3.33; N, 7.42; mol wt (mass spectroscopy), 191.

2-Amino-4-fluoronaphthalene. Prepared from the corresponding nitro compound in the same way as the 2,6 isomer, the amine crystallized from aqueous ethanol in needles, mp 44–45.5°.

Anal. Calcd for $C_{10}H_8NF$: C, 74.52; H, 5.00; N, 8.69; mol wt, 161. Found: C, 74.73; H, 5.18; N, 8.61; mol wt (mass spectroscopy), 161.

2-Acetamido-4-fluoronaphthalene. The acetyl derivative, after recrystallization from aqueous ethanol, and then ethyl acetate–petroleum ether, had mp 133–134°.

Anal. Calcd for $C_{12}H_{10}NOF$: C, 70.92; H, 4.96; N, 6.89; mol wt, 203. Found: C, 70.88; H, 4.97; N, 6.81; mol wt (mass spectroscopy), 203.

2-Bromo-4-fluoronaphthalene. 1-Amino-4-fluoronaphthalene (30 g) was brominated by the method used by Adcock and Wells[3] for 1-amino-4-methylnaphthalene. The dried hydrobromide was dissolved in ethanol and poured into a chilled solution of sodium bicarbonate. The black tarry precipitate was collected and extracted with boiling light petroleum, 40–60° (2 l.). The extract was decolorized with Norit and concentrated, yielding long pale purple needles, mp 58–63°. Thermal-gradient sublimation on a 100-mg sample of this crude material and subsequent mass spectral analysis showed the presence of three compounds: (a) unchanged 1-amino-4-fluoronaphthalene, (b) 1-amino-2-bromo-4-fluoronaphthalene, and (c) a dibromo derivative of a. The orientation of b followed from analogy;[3] presumably c is a monobromo derivative of b. Analysis by glpc indicated that b was the major component.

Three recrystallizations from petroleum ether (bp 40–60°) removed unchanged 1-amino-4-fluoronaphthalene; the residue (19 g) was deaminated by the procedure used for 1-amino-2-nitro-4-fluoronaphthalene, steam distilled, and then fractionally distilled. 2-Bromo-4-fluoronaphthalene was collected at 74–78° (0.3 mm) as a pale yellow oil (6.9 g), $n^{21}D$ 1.6314, homogeneous to glpc.

Anal. Calcd for $C_{10}H_6FBr$: mol wt, 225. Found: mol wt (mass spectroscopy), 224, 226.

The pot residue from the above distillation, after decolorizing with Norit, crystallized from ethanol in white needles of 2,*x*-dibromo-4-fluoronaphthalene, mp 101–102°.

Anal. Calcd for $C_{10}H_5FBr_2$: C, 39.47; H, 1.64; mol wt, 304. Found: C, 39.59; H, 1.71; mol wt (mass spectroscopy), 304.

2-Cyano-4-fluoronaphthalene. Prepared from the bromo isomer in the usual manner, the nitrile separated from Skellysolve B in needles, mp 121–122°.

Anal. Calcd for $C_{11}H_6NF$: C, 77.18; H, 3.53; N, 8.18; mol wt, 171. Found: C, 77.07; H, 3.73; N, 8.29; mol wt (mass spectroscopy), 171.

4-Fluoro-2-naphthoic Acid. Prepared by hydrolysis of the nitrile and purified by sublimation at 190° (1 mm), the acid crystallized from aqueous ethanol in fluffy needles, mp 189–191.5°.

Anal. Calcd for $C_{11}H_7O_2F$: C, 69.47; H, 3.68; mol wt, 190. Found: C, 69.62; H, 3.73; mol wt (mass spectroscopy), 190.

3-Fluoro-1-naphthoic Acid. 3-Nitro-1-naphthoic acid, mp 263–265° (lit.[18] 270.5–271.5°), was converted with methanolic sulfuric acid to the methyl ester, pale yellow needles (from methanol), mp 139–141°. This was reduced as usual to pale yellow methyl 3-amino-1-naphthoate, mp 69–71° (lit.[19] 72–73°). The amine ester was converted *via* the diazonium hexafluorophosphate (mp 143.5–144.5° dec) to methyl 3-fluoro-1-naphthoate which was isolated by steam distillation and then hydrolyzed to the acid with alcoholic potassium hydroxide. Additional material was recovered from the residue from the steam distillation by acidification, the total yield of 3-fluoro-1-naphthoic acid being 50%. A sample, after sublimation at 190° (1 mm), crystallized from aqueous ethanol in needles, mp 185–186°.

Anal. Calcd for $C_{11}H_7O_2F$: C, 69.47; H, 3.68. Found: C, 69.70; H, 3.84.

1-Amino-3-fluoronaphthalene. A solution of 3-fluoro-1-naphthoic acid (20 g, 0.11 mole) in chloroform (240 ml) was warmed with concentrated sulfuric acid (100 ml) to 40°, while powdered sodium azide (10.2 g) was added over 4 hr. After reaction was complete, the chloroform was decanted, the acid layer poured onto ice with vigorous stirring and basified with ammonium hydroxide, and the 1-amino-3-fluoronaphthalene isolated with ether and fractionated under reduced pressure, forming an almost colorless oil, bp 105–110° (0.5 mm), $n^{21}D$ 1.6410, which eventually solidified, mp 41–43°. Homogeneity was confirmed by glpc.

Anal. Calcd for $C_{10}H_8NF$: mol wt, 161. Found: mol wt (mass spectroscopy), 161.

1-Acetamido-3-fluoronaphthalene. The acetyl derivative crystallized from aqueous ethanol in needles, mp 166–167°.

Anal. Calcd for $C_{12}H_{10}ONF$: C, 70.92; H, 4.96; N, 6.89. Found: C, 71.14; H, 5.03; N, 6.95.

1-Dimethylamino-3-fluoronaphthalene. Prepared from 1-amino-3-fluoronaphthalene in the same way as the 1,7 isomer, the amine distilled as a colorless oil at 88–90° (0.5 mm), $n^{25}D$ 1.5942. Homogeneity was confirmed by glpc.

Anal. Calcd for $C_{12}H_{12}NF$: mol wt, 189. Found: mol wt (mass spectroscopy), 189.

1-Bromo-3-fluoronaphthalene. Prepared in the usual manner from 1-amino-2-fluoronaphthalene, 1-bromo-3-fluoronaphthalene was obtained as a colorless oil, bp 78–79° (0.5 mm), $n^{22}D$ 1.6250, homogeneous to glpc.

Anal. Calcd for $C_{10}H_6FBr$: mol wt, 225. Found: mol wt (mass spectroscopy), 224, 226.

2-Fluoro-4-nitronaphthalene. 1-Amino-3-fluoronaphthalene (8 g) was diazotized and excess acid neutralized with finely divided calcium carbonate. The solution was filtered, and the yellow diazonium cobaltinitrite was precipitated with sodium cobaltinitrite. The dried salt was decomposed using the procedure of Hodgson and Marsden,[20] giving 2-fluoro-4-nitronaphthalene which after steam distillation crystallized from Skellysolve B in pale yellow needles (1.5 g), mp 71.5–73°.

Anal. Calcd for $C_{10}H_6O_2NF$: C, 62.83; H, 3.16; N, 7.33. Found: C, 63.02; H, 3.30; N; 7.59.

1-Cyano-3-fluoronaphthalene. Prepared from the corresponding amine in the usual manner and isolated by steam distillation, the nitrile crystallized from Skellysolve B in needles, mp 101.5–102.5°.

Anal. Calcd for $C_{11}H_6NF$: C, 77.18; H, 3.53; N, 8.18. Found: C, 77.33; H, 3.71; N, 8.14.

1-Fluoro-6-nitronaphthalene. Following the procedure used for 3-fluoro-1-naphthoic acid, 6-nitro-1-naphthoic acid, mp 222–224° (lit.[18] 227–227.5°), was converted in 92% yield to the deep orange-

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(18) G. J. Leuck, R. P. Perkins, and F. C. Whitmore, *J. Am. Chem. Soc.*, **51**, 1831 (1929).

(19) R. Gould and W. A. Jacobs, *J. Biol. Chem.*, **130**, 407 (1939).

(20) H. H. Hodgson and E. Marsden, *J. Chem. Soc.*, 22 (1944).

red 1-amino-6-nitronaphthalene, mp 167–170° (lit.[18] 172–173°). The amine was converted *via* the diazonium hexafluorophosphate, mp 134–135° dec, to 1-fluoro-6-nitronaphthalene, which after steam distillation crystallized from Skellysolve B in lemon yellow needles, mp 109–110.5°.

Anal. Calcd for $C_{10}H_6O_2NF$: C, 62.83; H, 3.16; N, 7.33. Found: C, 62.97; H, 3.12; N, 7.35.

2-Amino-5-fluoronaphthalene. Reduction of the nitro compound in the usual way gave 2-amino-5-fluoronaphthalene as a colorless oil, bp 95–96° (0.3–0.4 mm), $n^{25}D$ 1.6440, homogeneous to glpc.

Anal. Calcd for $C_{10}H_8NF$: mol wt, 161. Found: mol wt (mass spectroscopy), 161.

2-Acetamido-5-fluoronaphthalene. The acetyl derivative crystallized from aqueous ethanol (Norit) and then from Skellysolve B–ethyl acetate as a white powder, mp 135.5–137°.

Anal. Calcd for $C_{12}H_{10}ONF$: C, 70.92; H, 4.96; N, 6.89. Found: C, 70.86; H, 5.13; N, 6.88.

2-Cyano-5-fluoronaphthalene. Prepared from the corresponding amine in the usual manner and isolated by steam distillation, the amine crystallized from Skellysolve B (Norit) in needles, mp 102–103°.

Anal. Calcd for $C_{11}H_6NF$: C, 77.18; H, 3.53. Found: C, 77.04; H, 3.72.

2-Bromo-5-fluoronaphthalene. Prepared from the corresponding amine in the usual manner and purified by preparative glpc (SE on Chromosorb W), this formed a colorless oil, $n^{25}D$ 1.6300.

Anal. Calcd for $C_{10}H_6FBr$: mol wt, 225. Found: mol wt (mass spectroscopy), 224, 226.

6-Fluoro-1-naphthoic Acid. Ethyl 6-nitro-1-naphthoate, mp 109–110° (lit.[18] 111.5–112°), was reduced in the usual manner, and the amine was converted to the diazonium hexafluorophosphate, mp 110.5–111.5° dec. This salt was decomposed by heating alone, and the resulting residue was treated overnight with alcoholic potassium hydroxide. The solution was then diluted, filtered, and acidified, giving 6-fluoro-1-naphthoic acid which after sublimation at 200° (1 mm) crystallized from aqueous ethanol in needles, mp 238–240.5°.

Anal. Calcd for $C_{11}H_7O_2F$: C, 69.47; H, 3.68. Found: C, 69.26; H, 3.71.

2-Fluoro-8-nitronaphthalene. 2-Amino-8-nitronaphthalene[8] was converted to the diazonium hexafluorophosphate, mp 134–136° dec; this on decomposition in mineral oil at 150° gave 2-fluoro-8-nitronaphthalene which crystallized from hexane in yellow needles, mp 85–86.5°.

Anal. Calcd for $C_{10}H_6O_2NF$: C, 62.83; H, 3.16; N, 7.33. Found: C, 63.00; H, 3.27; N, 7.41.

Substituent Effects. IX.[1] ^1H and ^{19}F Nuclear Magnetic Resonance Spectra of 4-Substituted 3,5-Dimethylfluorobenzenes[2]

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Abstract: ^{19}F chemical shifts are reported for a series of 4-substituted 3,5-dimethylfluorobenzenes (I); comparison of these values with ones for *para*-substituted fluorobenzenes show differences that can be attributed to steric hindrance of mesomerism. Combined with the arguments of part VII,[4] these results suggest that the π-inductive effect is not important, π polarization being mainly due to mesomeric interactions. The proton nmr spectra of I are also reported; it is pointed out that proton SCS values cannot be interpreted in terms of "normal" substituent theory, because of complications due to long-range magnetic interactions.

Previous papers[4–6] of this series have presented evidence suggesting that substituents influence the ^{19}F nmr chemical shifts of aryl fluorides in two main ways: first, by a direct electrostatic polarization of the C–F bond (field effect); secondly, by altering the π density at the carbon atom adjacent to fluorine. As one might expect on this basis, the field effect depends not only on the distance separating the substituent from fluorine, but also on its angular orientation; the factor determining the degree of polarization of the C–F bond is apparently the vector potential along its axis.

One point which still remains to be settled is the manner in which substituents can polarize the π system of an adjacent aromatic ring. Such a polarization could be produced either by a normal mesomeric interaction in cases where the substituent carries *para* or π electrons, or by a π-inductive effect; both these effects should lead to a qualitatively similar[7] π polarizations and it is therefore difficult to distinguish between them.

In part V,[6] an attempt was made to assess the importance of the π-inductive effect by studying the influence of CF_3, a powerful $+I$ substituent which cannot undergo normal mesomeric interactions; the results presented there seemed to suggest that the π-inductive effect is not important. The same conclusion follows from the success of the modified *FM* treatment of substituent effects in part VII,[4] where the π polarization was assumed to follow quantitatively the pattern calculated for a mesomeric effect.

However, neither of these arguments was conclusive, and we therefore decided to study the relative roles of the mesomeric and π-inductive effects by a more direct method. This can be done in the case of bulky substituents such as NO_2 or NMe_2 by introducing groups into the positions *ortho* to them; the resulting steric hindrance twists the substituent out of coplanarity with the ring and so interrupts conjugative interaction between the ring and the substituents. We have accordingly prepared a number of 4-substituted 3,5-

(1) Part VIII: W. Adcock and M. J. S. Dewar, *J. Am. Chem. Soc.*, **89**, 386 (1967).

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(5) M. J. S. Dewar and A. P. Marchand, *ibid.*, **88**, 354 (1966).

(6) M. J. S. Dewar and A. P. Marchand, *ibid.*, **88**, 3318 (1966).

(7) See M. J. S. Dewar, *ibid.*, **74**, 3350 (1952).