Derivatives of fluorene. XXV. Fluorofluorenes. VI[1-3]

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The synthesis of 5,6,7,8-tetrafluoro-2-acetamidofluorene, 1,4,7-trifluoro-2-acetamidofluorene, and 5,8-difluoro-2-acetamidofluorene, of a 1,2,3,4,7-penta-, a 1,2,3,4-tetra-, a 1,2,4,7-tetra-, a 1,4,7-tri-, and a 1,4-di-fluorofluorenone, and of related derivatives is reported together with their infrared absorption data. Nitration of polyfluorofluorenones which have an unsubstituted 2 (or 7) position occurs at that position. An unexpected directive effect was observed in the nitration of 4,7-difluoro-2-acetamidofluorene.

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Continuing our work on the synthesis of fluorinated derivatives of *N*-2-fluorenylacetamide for use in the exploration of carcinogenic mechanisms,[4] we have prepared a new difluoro (5,8-) (IV), one trifluoro (1,4,7-) (XIII), and one tetrafluoro (5,6,7,8-) (XX) derivative. It has been suggested, with some evidence (4), that the oxidation of certain *o*-aminophenols, including 2-amino-1-fluorenol, a metabolite of the carcinogen *N*-2-fluorenylacetamide, and the binding of the resulting *o*-quinoneimines to cellular components may be related to the mechanism of carcinogenic activity of these compounds. An end product of the oxidation of 2-amino-1-fluorenol by cytochrome *c* and cytochrome oxidase was identified (5) as 2-amino-1,4-fluorenoquinone-*N*^{4}-(1-hydroxy-2-fluorenyl)imine. In view of the above hypothesis and the experimental results, the synthesis and testing of *N*-2-(1,4,7-trifluorofluorenyl)acetamide (XIII) are particularly pertinent because the 1 and 4 positions and, in addition, the chief hydroxylation (detoxification?) site, the 7 position, are blocked. It was reported earlier (2) that *N*-2-(7-fluorofluorenyl)-acetamide is a more potent liver carcinogen in male rats than *N*-2-fluorenylacetamide itself.

The Ullmann reaction between 2,5-difluoroiodobenzene (which was prepared from 2,5-difluoroaniline) and methyl *o*-bromobenzoate, using the improved procedure described earlier (1), followed by ring closure, yielded 1,4-difluoro-9-oxofluorene (I) in a 48% yield.

Nitration of I gave a good yield of 5,8-difluoro-2-nitro-9-oxofluorene (II). One-step double reduction (nitro group and 9-keto group) with hydriodic acid and red phosphorus (1) gave an excellent yield of the difluorofluorenamine III.

Reduction of II with stannous chloride dihydrate and hydrochloric acid gave the corresponding aminofluorenone VI. Diazotization of the aminofluorenone VI in the presence of dimethyl sulfoxide (1, 6), followed by Schiemann decomposition, yielded 9-oxo-1,4,7-trifluorofluorene (VIII). Nitration gave 2-nitro-9-oxo-1,4,7-trifluorofluorene (IX). This was also successfully reduced to the aminofluorene XII, in one step, with hydriodic acid and red phosphorus. The structures of the foregoing compounds were confirmed as shown in Scheme 1. The key compound in this proof was 9-oxo-1,2,4,7-tetrafluorofluorene (XIV), made in two ways.

The Ullmann coupling of methyl *o*-bromobenzoate and 2,3,4,5-tetrafluoroiodobenzene

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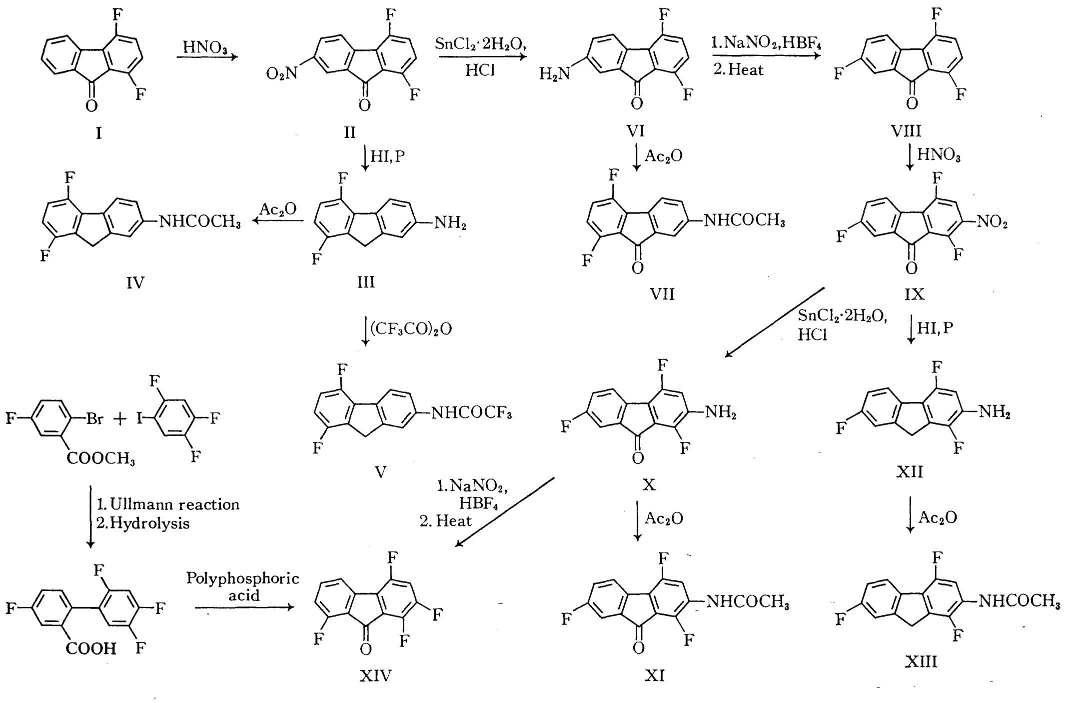
[1] For part XXIV in this series, see H. L. Pan and T. L. Fletcher, J. Med. Chem. **10**, 957 (1967).

[2] For sub-part V in this series, see ref. 1.

[3] This work was supported in part by research grant CA-01744 from the National Cancer Institute and by career development award 5-K3-CA-14,991 (to T. L. F.) from the National Institutes of Health, U.S.P.H.S.

[4] The biological work on these compounds is being carried out by Drs. J. A. and E. C. Miller and their associates at the McArdle Laboratory for Cancer Research, University of Wisconsin, Madison. The results from some of the earlier compounds and the rationale for testing this series have been published (2, 3).



SCHEME 1.

(prepared from 2,3,4,5-tetrafluoroaniline[5]), followed by ring closure, gave 9-oxo-1,2,3,4-tetrafluorofluorene (XV) in nearly a 70% yield. Nitration of XV gave 2-nitro-9-oxo-5,6,7,8-tetrafluorofluorene (XVI). The position of the nitro group was confirmed in a manner similar to that outlined in Scheme 1 for the nitrotrifluorofluorenone IX. One-step reduction of XVI by hydriodic acid and red phosphorus gave an excellent yield of 5,6,7,8-tetrafluorofluoren-2-amine (XIX).

Upon mononitration of *N*-2-fluorenylacetamide, substitution takes place mainly at the 3 and 7 positions (7–9), and very slightly (<1%) at the 1 position (10). When the 7 position is blocked by a nitro (11) or a fluoro (12) group, substitution takes place mainly[6] at the 3 position. However, when *N*-2-(4,7-difluorofluorenyl)-acetamide (XXII) (1) is nitrated, the nitro group enters the 1 position, giving a high yield. The nitrated product was oxidized to the fluorenone XXIV; hydrolysis followed by deamination gave 1-nitro-4,7-difluorofluorenone (XXV). The position of the nitro group was confirmed, as shown in Scheme 2, when the nitro compound was reduced to the amine XXVI and converted into VIII, which was identical with the compound prepared from I as shown in Scheme 1.

EXPERIMENTAL

Melting points were taken on a Fisher–Johns block and are corrected. Analyses were carried out by Schwarzkopf Microanalytical Laboratory, Woodside, New York, and by Dr. A. Bernhardt, Mülheim, Germany. Infrared spectra were obtained with a Beckman IR-5 spectrophotometer, using KBr disks for solid samples (ca. 1.5 mg/300 mg of KBr) and films between NaCl plates for liquids. The infrared absorption bands for C—F stretching are tentatively assigned and are a continuation of previous work in this laboratory (see, for example, refs. 1 and 12).

Preparation of 2,5-Difluoroiodobenzene

A hot (110°) solution of 194 g (1.5 moles) of 2,5-difluoroaniline (Pierce Chemical Co.) in 400 ml of

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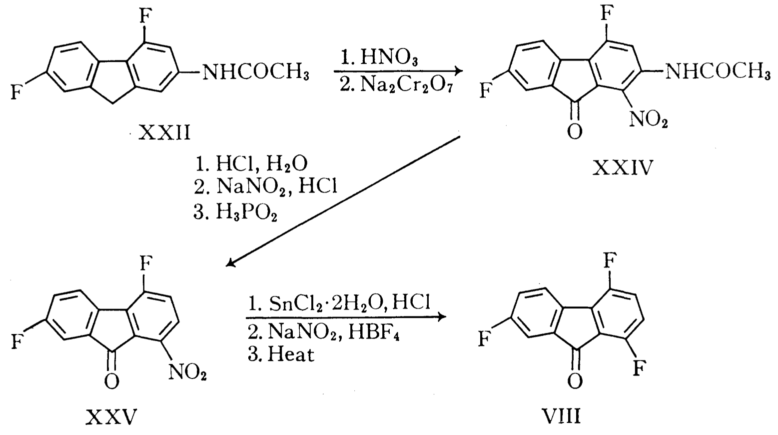
[5] Some of this compound was generously supplied by Dr. Harry B. Wood, Jr. of the Cancer Chemotherapy National Service Center, N.I.H.

[6] The product is obtained readily in the first crop in a reasonably pure form.



SCHEME 2.

concentrated hydrochloric acid and 100 ml of water was cooled to 10° in an ice bath. Crushed ice (300 g) was added, with stirring, and when the temperature reached −5°, a saturated aqueous solution of 117 g (1.7 moles) of sodium nitrite was added slowly. The diazonium salt solution was stirred for 20 min in the ice bath and then added to a cooled (10°) solution of 400 g (2.4 moles) of potassium iodide in 400 ml of water. The dark heavy oil was separated, shaken with an aqueous solution of 40 g of sodium bisulfite, again separated, dried, and distilled, giving 238 g (66%) of the product, b.p. 68–69° at 14 mm, n_D^{25} 1.5593. The infrared spectrum had absorption peaks[7] at 1 247 (s) and 1 189 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_6H_3F_2I$: C, 30.03; H, 1.26; I, 52.88. Found: C, 30.25; H, 1.45; I, 52.79.

Preparation of 1,4-Difluoro-9-oxofluorene (I)

A mixture of 72 g (0.3 mole) of 2,5-difluoroiodobenzene, 194 g (0.9 mole) of methyl *o*-bromobenzoate, and 90 g of copper powder[8] was placed in an Ullmann reactor (1) and slowly heated to 200 ±5 ° during 1.5 h, with rapid stirring. This temperature was maintained throughout the reaction. After the mixture was stirred for a further 2.5 h, 45 g of copper powder was added; this was repeated after another hour. Stirring was continued for 2.5 h. The usual procedure (1) gave 31.5 g (48%) of the product, m.p. 154–159°. One recrystallization from ethanol raised the melting point to 158.5–159.5°. An analytical sample was prepared by a further recrystallization from benzene, m.p. 159–159.5°. The infrared spectrum had absorbtion peaks at 1 718 (s) (keto C═O), 1 245 (s) and 1 232 (s) (C—F), and 768 (m) and 741 (s) (four adjacent protons on phenyl) cm^{-1}.

Anal. Calcd. for $C_{13}H_6F_2O$: C, 72.22; H, 2.80; F, 17.58. Found: C, 72.32; H, 2.93; F, 17.81.

Preparation of 5,8-Difluoro-2-nitro-9-oxofluorene (II)

After the addition of 45 g (0.206 mole) of I to 90 ml of nitric acid (90%), the temperature being kept below 50°, the mixture was worked up in the usual way, followed by recrystallization from toluene (Darco), to give 46 g (85%) of II, m.p. 228–229°. An analytical sample, with the same melting point, was prepared by another recrystallization from toluene. The infrared spectrum had absorption peaks at 1 724 (s) (keto C═O), 1 524 (s) and 1 350 (s) (NO$_2$), and 1 350 (s) and 1 241 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{13}H_5F_2NO_3$: C, 59.78; H, 1.93; F, 14.55; N, 5.36. Found: C, 59.70; H, 2.16; F, 14.75; N, 5.51.

Preparation of 5,8-Difluorofluoren-2-amine (III)

A mixture of 26.1 g (0.1 mole) of II, 100 g of red phosphorous, 140 ml of hydriodic acid (55–58%), and 1 200 ml of glacial acetic acid was refluxed for 42 h. The mixture was then evaporated to near dryness, 1 400 ml of boiling water was added, the mixture was filtered while hot, and the filtrate was basified with ammonium hydroxide. The resulting white precipitate was filtered off, washed, and dried, giving 21.3 g (98%) of the product, m.p. 132–134°. Recrystallization from ethanol (Darco) yielded 17.6 g (81%), m.p. 134–135°. The infrared spectrum had absorption peaks at 3 460 (s) and 3 367 (s) (NH$_2$) and 1 258 (m) and 1 221 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{13}H_9F_2N$: C, 71.88; H, 4.17; F, 17.50; N, 6.45. Found: C, 71.73; H, 4.30; F, 17.70; N, 6.60.

Preparation of N-2-(5,8-Difluorofluorenyl)acetamide (IV)

Acetylation of III gave a 100% yield of IV, m.p. 200–201.5°. Recrystallization from ethanol raised this to 200.5–201.5°. The infrared spectrum had absorption peaks at 1 658 (s) (amide C═O) and 1 250 (m) and 1 225 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{15}H_{11}F_2NO$: C, 69.49; H, 4.28; F, 14.66; N, 5.40. Found: C, 69.31; H, 4.24; F, 14.87; N, 5.53.

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[7] Abbreviations used: s, strong; m, medium.

[8] Obtained from Metals Disintegrating Co. (grade H50A).

Preparation of N-2-(5,8-Difluorofluorenyl)-2′,2′,2′-trifluoroacetamide (V)

Reaction of III with trifluoroacetic anhydride in benzene gave the amide V, m.p. 188–189°. An analytical sample was prepared by recrystallization from ethanol (Darco), m.p. 189–189.5°. The infrared spectrum had absorption peaks at 1 704 (s) (amide C=O), 1 250 (m) and 1 230 (s) (C—F), and from 1 205 to 1 160 (broad s) (CF_3) cm^{-1}.

Anal. Calcd. for $C_{15}H_8F_5NO$: C, 57.51; H, 2.58; N, 4.47. Found: C, 57.45; H, 2.54; N, 4.47.

Preparation of 5,8-Difluoro-9-oxofluoren-2-amine (VI)

Reduction of II with stannous chloride dihydrate and hydrochloric acid in the usual way gave an 80% yield of VI after one recrystallization from toluene, m.p. 211–213°. An analytical sample was prepared by recrystallization from ethanol, m.p. 212–213°. The infrared spectrum had absorption peaks at 3 448 (s) and 3 356 (s) (NH_2), 1 704 (s) (keto C=O), and 1 242 (m) and 1 230 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{13}H_7F_2NO$: C, 67.55; H, 3.05; F, 16.44; N, 6.06. Found: C, 67.37; H, 3.06; F, 16.36; N, 6.03.

Preparation of N-2-(5,8-Difluoro-9-oxofluorenyl)-acetamide (VII)

Acetylation of VI in the usual way gave VII, m.p. 300–303°. Recrystallization from ethanol gave an analytical sample, m.p. 302–303°. The infrared spectrum had absorption peaks at 1 715 (s) (keto C=O), 1 692 (s) (amide C=O), and 1 245 (s) and 1 232 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{15}H_9F_2NO_2$: C, 65.93; H, 3.32; N, 5.13. Found: C, 66.11; H, 3.39; N, 5.31.

Preparation of 9-Oxo-1,4,7-trifluorofluorene (VIII)

(*a*) Diazotization of 46.2 g (0.2 mole) of VI in 200 ml of dimethyl sulfoxide with 500 ml of 50% fluoboric acid and 23 g (0.33 mole) of $NaNO_2$ gave a quantitative yield of the diazonium salt, decomposition point 172 – 175°. Decomposition in boiling *o*-dichlorobenzene gave 38 g of the product, m.p. 174–180°. Recrystallization from ethanol yielded 31 g (67%), m.p. 180–181°. An analytical sample was prepared by sublimation at 165° and 1 mm, followed by recrystallization from ethanol, m.p. 181–181.5°. The infrared spectrum had absorption peaks at 1 724 (s) (keto C=O), 1 269 (s), 1 244 (s), and 1 215 (s) (C—F), 873 (s) (isolated proton on phenyl), and 834 (s) and 819 (s) (two adjacent protons on phenyl) cm^{-1}.

Anal. Calcd. for $C_{13}H_5F_3O$: C, 66.67; H, 2.15; F, 24.24. Found: C, 66.80; H, 2.34; F, 24.28.

(*b*) Diazotization of 4,7-difluoro-9-oxofluoren-1-amine (XXVI)[9] as in method *a* gave a salt, decomposition point 180°. Schiemann decomposition of the salt gave the product, m.p. 178–181°. Sublimation at 170° and 1 mm raised the melting point to 180.5–181.5°. Admixture with the product obtained by method *a* did not depress the melting point, and the infrared spectra of both products were identical.

Preparation of 2-Nitro-9-oxo-1,4,7-trifluorofluorene (IX)

To 35 ml of 90% nitric acid in a beaker at room temperature, 23.4 g (0.1 mole) of VIII was added in portions, with stirring. The rate of addition was regulated to keep the temperature from rising above 35°. After the addition was completed, the mixture was heated briefly to 40° and allowed to cool to room temperature, at which point a yellow solid precipitated. The mixture was poured into 200 ml of water, and the precipitate was removed by filtration, washed with water, and dried, giving 27.5 g (98%), m.p. 215–220°. Recrystallization from toluene (Darco) gave 22 g (79%), m.p. 220–220.5°. An analytical sample, with the same melting point, was prepared by sublimation at 200° and 1 mm. The infrared spectrum had absorption peaks at 1 721 (s) (keto C=O), 1 531 (s) and 1 337 (s) (NO_2), and 1 261 (s) and 1 220 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{13}H_4F_3NO_3$: C, 55.93; H, 1.44; F, 20.42; N, 5.02. Found: C, 55.94; H, 1.53; F, 20.34; N, 5.21.

Preparation of 9-Oxo-1,4,7-trifluorofluoren-2-amine (X)

Reduction of 1.8 g of IX with 7 g of stannous chloride dihydrate and 10 ml of hydrochloric acid in the usual way gave 1.2 g (74%) of X after one recrystallization from toluene, m.p. 235–236°. An analytical sample was prepared by recrystallization from ethanol, m.p. 235.5–236°. The infrared spectrum had absorption peaks at 1 709 (s) (keto C=O), 1 282 (s), 1 255 (s), and 1 227 (s) (C—F), 858 (m) (isolated proton on phenyl), and 790 (s) (two adjacent protons on phenyl) cm^{-1}.

Anal. Calcd. for $C_{13}H_6F_3NO$: F, 22.87; N, 5.62. Found: F, 22.52; N, 5.65.

Preparation of N-2-(9-Oxo-1,4,7-trifluorofluorenyl)-acetamide (XI)

Acetylation of X gave the amide, m.p. 267–268°. Recrystallization from ethanol raised the melting point to 267.5–268°. The infrared spectrum had absorption peaks at 1 724 (s) (keto C=O), 1 686 (s) (amide C=O), and 1 267 (s), 1 247 (s), and 1 211 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{15}H_8F_3NO_2$: C, 61.86; H, 2.77; N, 4.81. Found: C, 61.88; H, 2.68; N, 5.09.

Preparation of 1,4,7-Trifluorofluoren-2-amine (XII)

Reduction of 20 g of IX with hydriodic acid (55–58%) and red phosphorus gave 14.8 g (87%) of XII, m.p. 108–110°. Recrystallization from ethanol (Darco) gave an analytical sample, m.p. 109–110°. The infrared spectrum had absorption peaks at 3 425 (s) and 3 333 (s) (NH_2) and 1 258 (s), 1 235 (s), and 1 209 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{13}H_8F_3N$: C, 66.38; H, 3.43; F, 24.23; N, 5.96. Found: C, 66.26; H, 3.42; F, 24.15; N, 6.11.

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[9] The synthesis of this amine is described later in this paper.

Preparation of N-2-(1,4,7-Trifluorofluorenyl)-acetamide (XIII)

Acetylation of XII in benzene gave a quantitative yield of XIII, m.p. 213–215°. Recrystallization from ethanol (Darco) raised the melting point to 215–215.5°. The infrared spectrum had absorption peaks at 1 664 (s) (amide C=O) and 1 282 (s), 1 276 (s), and 1 235 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{15}H_{10}F_3NO$: C, 64.98; H, 3.64; F, 20.56; N, 5.05. Found: C, 65.05; H, 3.83; F, 20.49; N, 5.14.

Preparation of 2,4,5-Trifluoroiodobenzene

Diazotization of 23 g of 2,4,5-trifluoroaniline (13) with hydrochloric acid and sodium nitrite and subsequent treatment with aqueous potassium iodide solution, as described in the procedure for making 2,5-difluoroiodobenzene, gave 32 g (80%) of the crude product. Distillation gave pure 2,4,5-trifluoroiodobenzene, b.p. 66–67° at 17 mm, n_D^{25} 1.5349. The infrared spectrum had absorption peaks at 1 312 (s), 1 276 (s), and 1 193 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_6H_2F_3I$: C, 27.93; H, 0.78; F, 22.10; I, 49.19. Found: C, 28.12; H, 0.85; F, 21.93; I, 48.81.

Preparation of 9-Oxo-1,2,4,7-tetrafluorofluorene (XIV)

(*a*) An Ullmann condensation, as described above, between 2,4,5-trifluoroiodobenzene and methyl 2-bromo-5-fluorobenzoate (14) yielded 50% of XIV after sublimation at 130° and 1 mm, m.p. 141–142°. The infrared spectrum had absorption peaks at 1 724 (s) (keto C=O), 1 295 (s), 1 267 (s), and 1 220 (s) (C—F), 863 (m) (isolated proton on phenyl), and 787 (s) (two adjacent protons on phenyl) cm^{-1}.

Anal. Calcd. for $C_{13}H_4F_4O$: C, 61.91; H, 1.59; F, 30.13. Found: C, 62.02; H, 1.69; F, 29.87.

(*b*) Diazotization of X with fluoboric acid (50%) and sodium nitrite in the presence of dimethyl sulfoxide at −5° and subsequent thermal decomposition of the diazonium fluoborate salt at 300° gave XIV in a 20% yield based on the amine. After sublimation at 130° and 1 mm and recrystallization from ethanol, the melting point was 141–142°. Admixture with the product obtained by method *a* did not depress the melting point, and the infrared spectra of both products were identical.

Preparation of 2,3,4,5-Tetrafluoroiodobenzene

Diazotization of 82.5 g (0.5 mole) of 2,3,4,5-tetrafluoroaniline[5] (Imperial Smelting Corp., Ltd.) with hydrochloric acid and sodium nitrite and subsequent treatment with aqueous potassium iodide solution, as described in the procedure for making 2,5-difluoroiodobenzene, gave 115 g (83%) of the crude product. Distillation gave 87 g, b.p. 47–49° at 6 mm, n_D^{25} 1.5137. The infrared spectrum had absorption peaks at 1 321 (m), 1 200 (s), 1 091 (s), and 1 001 (s) (C—F) and 852 (s) (isolated proton on phenyl) cm^{-1}.

Anal. Calcd. for C_6HF_4I: C, 26.11; H, 0.36; I, 45.99. Found: C, 26.27; H, 0.46; I, 45.96.

Preparation of 9-Oxo-1,2,3,4-tetrafluorofluorene (XV)

An Ullmann condensation of 82.7 g (0.3 mole) of 2,3,4,5-tetrafluoroiodobenzene and methyl *o*-bromobenzoate, as described for I, yielded 51 g (67%) of the product, m.p. 145–147°. Sublimation at 140° and 1 mm yielded 46 g of the pure compound, m.p. 147.5–148°. The infrared spectrum had absorption peaks at 1 718 (s) (keto C=O), 1 316 (s), 1 304 (s), 1 129 (s), and 1 059 (s) (C—F), and 773 (s) and 743 (s) (four adjacent protons on phenyl) cm^{-1}.

Anal. Calcd. for $C_{13}H_4F_4O$: C, 61.91; H, 1.59; F, 30.13. Found: C, 61.96; H, 1.65; F, 30.04.

Preparation of 2-Nitro-9-oxo-5,6,7,8-tetrafluorofluorene (XVI)

To 50 ml of nitric acid (90%), 25.2 g (0.1 mole) of XV was added in small portions, with stirring. The temperature was not allowed to rise above 40°. After the addition, the mixture was heated briefly to 50° and allowed to cool to room temperature. When the mixture was poured into 200 ml of water, a light-yellow solid precipitated; this was filtered off, washed, and dried, giving 29.7 g (100%) of the crude product, m.p. 168–170°. Recrystallization from toluene (Darco) gave 26.4 g (89%), m.p. 170–171°. An analytical sample, with the same melting point, was prepared by recrystallization from ethanol. The infrared spectrum had absorption peaks at 1 721 (s) (keto C=O), 1 531 (s) and 1 355 (s) (NO_2), and 1 311 (s), 1 133 (s), and 1 058 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{13}H_3F_4NO_3$: C, 52.52; H, 1.02; N, 4.71. Found: C, 52.68; H, 1.20; N, 4.96.

Preparation of 9-Oxo-5,6,7,8-tetrafluorofluoren-2-amine (XVII)

A mixture of 5 g of XVI, 28 ml of concentrated hydrochloric acid, 20 ml of ethanol, and 28 g of stannous chloride dihydrate was boiled for 10 min. A vigorous reaction took place, followed by deposition of a yellow precipitate. When the reaction mixture was cooled to room temperature, the precipitate was filtered off, washed with 10 ml of dilute hydrochloric acid, and suspended in 20 ml of dilute ammonium hydroxide. The dark-purple precipitate was filtered off, dried, and dissolved in 200 ml of boiling toluene. Inorganic material was filtered off, and the filtrate was concentrated to 100 ml and cooled. Filtration and drying gave 4.1 g (90%), m.p. 248–249°. An analytical sample, with the same melting point, was prepared by sublimation at 240° (metal bath) and 1 mm. The infrared spectrum had absorption peaks at 3 448 (s) and 3 356 (s) (NH_2), 1 704 (s) (keto C=O), and 1 325 (s), 1 302 (s), 1 253 (m), and 1 059 (m) (C—F) cm^{-1}.

Anal. Calcd. for $C_{13}H_5F_4NO$: C, 58.44; H, 1.89; F, 28.44; N, 5.24. Found: C, 58.40; H, 1.99; F, 28.45; N, 4.98.

Preparation of N-2-(9-Oxo-5,6,7,8-tetrafluorofluorenyl)acetamide (XVIII)

Acetylation of XVII in the usual way gave XVIII, m.p. 300–302°. Sublimation at 270–280° and 1 mm gave an analytical sample, m.p. 302–303°. The infrared spectrum had absorption peaks at 1 718 (s) (keto C=O), 1 695 (s) (amide C=O), and 1 403 (s), 1 314 (s), 1 093 (m), and 1 062 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{15}H_7F_4NO_2$: N, 4.53. Found: N, 4.71.

Preparation of 5,6,7,8-Tetrafluorofluoren-2-amine (XIX)

(*a*) A mixture of 1.2 g of XVII, 5 g of red phosphorus, 7 ml of hydriodic acid (55–58%), and 60 ml of glacial acetic acid was refluxed for 48 h and then evaporated to near dryness. Boiling water (70 ml) was added, the mixture was filtered, and the filtrate was basified with ammonium hydroxide. The resulting white precipitate was filtered off, washed, and dried, giving 1.1 g (97%), m.p. 142–149° (slight residue). Sublimation at 135–145° and 1 mm gave 1.05 g (93%), m.p. 148–149°. The infrared spectrum had absorption peaks at 3 448 (s) and 3 401 (s) (NH_2) and 1 328 (m), 1 289 (m), 1 269 (m), and 1 025 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{13}H_7F_4N$: C, 61.66; H, 2.79; N, 5.53. Found: C, 61.55; H, 2.86; N, 5.63.

(*b*) A mixture of 14.9 g (0.05 mole) of XVI, 50 g of red phosphorus, 70 ml of hydriodic acid (55–58%), and 600 ml of glacial acetic acid was refluxed for 42 h. The mixture was then treated as in method *a* to obtain a quantitative yield of the crude product. Recrystallization from ethanol (Darco) gave 11.3 g (89%), m.p. 148–149°. Admixture with the product prepared by method *a* did not depress the melting point.

Preparation of N-2-(5,6,7,8-Tetrafluorofluorenyl)-acetamide (XX)

Acetylation of XIX in benzene gave a quantitative yield, m.p. 231–233°. An analytical sample was obtained by two recrystallizations from ethanol (Darco), m.p. 232–233°. The infrared spectrum had absorption peaks at 1 664 (s) (amide C═O) and 1 289 (s), 1 266 (m), 1 109 (m), and 1 031 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{15}H_9F_4NO$: C, 61.02; H, 3.07; F, 25.74; N, 4.75. Found: C, 61.30; H, 2.98; F, 25.64; N, 4.50.

Preparation of 9-Oxo-1,2,3,4,7-pentafluorofluorene (XXI)

(*a*) To a solution of 2 g of XVII in 10 ml of dimethyl sulfoxide, 20 ml of 50% fluoboric acid was added; the yellow amine salt precipitated. The mixture was cooled to 5° in an ice bath, and 10 g of crushed ice was added. To the cold (−10°) mixture, aqueous sodium nitrite (1 g) was added and the mixture stirred for 10 min. The diazonium salt was filtered off, washed successively with 5 ml of dilute (5%) fluoboric acid, 5 ml of methanol, and 5 ml of ether, and dried, giving 2.5 g, decomposition point 160°. The salt was decomposed by adding it to boiling *o*-dichlorobenzene (20 ml). Evaporation of the solvent gave 1.3 g (65%) of the product, m.p. 145–147°. Sublimation at 130° and 1 mm gave 1.1 g, m.p. 148–149°. The infrared spectrum had absorption peaks at 1 715 (s) (keto C═O) and 1 305 (s), 1 263 (s), 1 121 (s), and 1 056 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{13}H_3F_5O$: C, 57.79; H, 1.12; F, 35.17. Found: C, 57.97; H, 1.30; F, 34.93.

(*b*) The Ullmann reaction between 13.8 g of 2,3,4,5-tetrafluoroiodobenzene and 47 g of methyl 2-bromo-5-fluorobenzoate (see the procedure for 1,4-difluoro-9-oxofluorene), according to the usual procedure, gave 3.2 g (25%) of XXI, m.p. 146–148°. Recrystallization from ethanol raised the melting point to 147.5–148.5°. A mixture melting point with the product prepared by method *a* was not depressed and the infrared spectra were identical.

Preparation of N-2-(4,7-Difluoro-1-nitrofluorenyl)-acetamide (XXIII)

A solution of 13 g (0.05 mole) of XXII (1) in 100 ml of acetic acid was cooled to 30°, and 25 ml of nitric acid (density 1.42) was added, with stirring. The temperature of the mixture rose to 42°, the solution turned dark, and a yellow solid precipitated. Recrystallization from toluene gave an analytical sample, (72%), m.p. 236–237°. The infrared spectrum had absorption peaks at 1 704 (s) (amide C═O), 1 534 (s) and 1 370 (s) (NO_2), and 1 266 (s) and 1 222 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{15}H_{10}F_3N_2O_3$: N, 9.21. Found: N, 9.27.

Preparation of N-2-(4,7-Difluoro-1-nitro-9-oxofluorenyl)acetamide (XXIV)

A mixture of 8.4 g of XXIII and 25 g of sodium dichromate in 170 ml of acetic acid was heated under reflux for 1 h and evaporated to 40 ml. After the reaction mixture had cooled, the precipitate was filtered off, washed with water, and dried, giving 8.1 g of yellow needles, m.p. 272–273°. One recrystallization from toluene gave an analytical sample, m.p. 273–274°. The infrared spectrum had absorption peaks at 1 718 (s) (keto C═O), 1 701 (s) (amide C═O), 1 534 (s) and 1 376 (s) (NO_2), and 1 269 (s) and 1 236 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{15}H_8F_2N_2O_4$: N, 8.80. Found: N, 9.05.

Preparation of 4,7-Difluoro-1-nitro-9-oxofluorene (XXV)

A mixture of 11 g of XXIV and 50 ml of concentrated sulfuric acid was heated on a steam bath for 1 h and then cooled to room temperature. To this solution, a nitrosyl sulfate solution (prepared by adding 2.5 g of sodium nitrite to 20 ml of concentrated sulfuric acid at room temperature) was added, with stirring. After the mixture was allowed to stand for 4 h, it was poured onto 50 g of cracked ice. To the diazonium salt mixture, 30 ml of 50% hypophosphorous acid was added, with stirring. Reaction took place smoothly, with the evolution of gas. The mixture was stirred for 1 h and then allowed to stand overnight. A brownish-yellow precipitate was filtered off, washed with water, and dried, giving 9 g (99%) of the product, m.p. 195–210°. Sublimation at 190° and 1 mm, followed by recrystallization from toluene, gave 6.6 g (73%), m.p. 212–213°. The infrared spectrum had absorption peaks at 1 727 (s) (keto C═O), 1 534 (s) and 1 359 (s) (NO_2), and 1 269 (s) and 1 250 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{13}H_5F_2NO_3$: C, 59.78; H, 1.93; N, 5.36. Found: C, 60.04; H, 1.90; N, 5.41.

Preparation of 4,7-Difluoro-9-oxofluoren-1-amine (XXVI)

Reduction of 3 g of XXV with 12 g of stannous chloride dihydrate, 20 ml of concentrated hydrochloric acid, and 10 ml of ethanol gave the amine (2.7 g), m.p. 184–185°. The infrared spectrum had absorption peaks at 1 686 (s) (keto C═O) and 1 269 (s) and 1 230 (s) (C—F) cm^{-1}.

Anal. Calcd. for $C_{13}H_7F_2NO$: N, 6.06. Found: N, 6.03.

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