182–187°. Recrystallization from benzene raised the m.p. to 186–187°. An analytical sample was prepared by sublimation at 180° (1 mm.), m.p. 187–187.5°; $\lambda_{max}$ 288 m$\mu$ ($\epsilon$ 8.20 $\times$ $10^3$), 327 (1.38 $\times$ $10^4$); C–F stretching: 8.17 $\mu$, 8.32. $\mu$.

*Anal.* Calcd. for $C_{13}H_7F_2NO_2$: C, 63.16; H, 2.85; N, 5.67. Found: C, 63.39; H, 3.29; N, 5.92.

(b) To a solution of 2.02 g. (0.01 mole) of 2,6-difluorofluorene in 8 ml. of glacial acetic acid at 50°, 2 ml. of nitric acid (d. 1.42) was added, the mixture was heated to 70° and 4 drops of concd. sulfuric acid were added with stirring. An exothermic reaction occurred with formation of a yellow precipitate. The temperature of the mixture was kept 85° for 5 min., then allowed to drop to 25°. The precipitate was filtered, washed with cold acetic acid and water, and dried, giving 2.2 g. (89%) of crude product, m.p. 182–186°. One recrystallization from benzene (Darco) gave 1.8 g. (73.5%) of the pure compound, m.p. 186–187°. A mixture melting point with the Schiemann decomposition product of 3-fluoro-2-nitro-7-fluorenamine was undepressed, and the infrared spectra of the two compounds were identical.

*2-Amino-3,7-difluorofluorene.* An alcoholic solution (50 ml.) of 0.46 g. (0.002 mole) of 2-nitro-3,7-difluorofluorene was reduced with 0.5 ml. of 100% hydrazine hydrate and Raney nickel[10] giving 0.38 g. (95%) of the amine, m.p. 124–124.5°. One recrystallization from alcohol gave an analytical sample, m.p. 124–124.5°; $\lambda_{max}$ 279 m$\mu$ ($\epsilon$ 1.97 $\times$ $10^4$), 326 (8.75 $\times$ $10^3$), C—F stretching: 8.01 $\mu$, 8.56 $\mu$.

*Anal.* Calcd. for $C_{13}H_9F_2N$: N, 6.45. Found: N, 6.28.

*N-2-(3,7-Difluorofluorenyl)acetamide.* The foregoing compound was acetylated quantitatively with acetic anhydride on the steam bath for 10 min. The product was recrystallized from alcohol (Darco), m.p. 240–240.5°; $\lambda_{max}$ 274 m $\mu$ ($\epsilon$ 2.03 $\times$ $10^4$), 308 (1.49 $\times$ $10^4$), $\lambda_{shoulder}$ 280 m$\mu$, 286 $\mu$; C–F stretching: 8.08 $\mu$, 8.57 $\mu$.

*Anal.* Calcd. for $C_{15}H_{11}F_2NO$: C, 69.49; H, 4.28; F, 14.66; N, 5.40. Found: C, 69.68; H, 4.28; F, 14.47; N, 5.40.

*1,7-Difluorofluorene.* A solution of 4.3 g. (0.0216 mole) of 1-fluoro-7-fluorenamine[5] in 25 ml. of tetrahydrofuran[9] and 25 ml. of 48–50% fluoboric acid (0°) was diazotized. After 30 min., the salt was filtered and washed giving 5.9 g. (91%), dec. 170°. This was suspended in *o*-dichlorobenzene and heated gradually to the boiling point. Upon evaporating the solvent and recrystallizing the residue from petroleum ether (b.p 30–60°), 2.7 g. (62%, based on the amine) of product was obtained, m.p. 64–66°. Two recrystallizations from cyclohexane followed by sublimation (75°, 1 mm.) gave an analytical sample, m.p. 73.5–74.5°; $\lambda_{max}$ 261 m$\mu$ ($\epsilon$ 1.84 $\times$ $10^4$), 278 (7.60 $\times$ $10^3$), 287 (3.67 $\times$ $10^3$), 299 (3.27 $\times$ $10^3$), $\lambda_{shoulder}$ 216 m$\mu$, 255, 271, 292; C—F stretching : 8.03 $\mu$, 8.13 $\mu$.

*Anal.* Calcd. for $C_{13}H_8F_2$: C, 77.22; H, 3.99; F, 18.79. Found: C, 77.35; H, 4.08; F, 18.67.

*Nitration of 1,7-difluorofluorene.* The foregoing compound (2 g., 0.001 mole) was nitrated in the same manner as above, giving 2.2 g. of crude product, m.p. 125–128°, three recrystallizations from alcohol raised the m.p. to 127–130°. A benzene solution of this was percolated through alumina and upon evaporating the solvent, 1.72 g. was recovered with melting point unchanged. The infrared spectrum of this material was almost the same as that of 2-nitro-1,7-difluorofluorene, described in the following section, with a few additional bands.

*2-Nitro-1,7-difluorofluorene.* To a solution of 3.85 g. (0.017 mole) of 1-fluoro-2-nitro-7-fluorenamine[6] in 30 ml. of tetrahydrofuran[9] 50 ml. of 50% fluoboric acid was added to form a thick white salt. This was cooled to 0° and a saturated aqueous solution of 2 g. (0.029 mole) of sodium nitrite was added dropwise with stirring. The resulting diazonium salt was filtered, washed as above, and dried, giving 4.5 g. (90%), dec. 140°. Upon decomposition in boiling xylene, evaporation of the liquid and recrystallization from alcohol (Darco) 2.8 g. (71% based on the amine) of the 2-nitro-1,7-difluorofluorene was obtained, m.p. 164–165°. An analytical sample was prepared by sublimation at 150° (1 mm.), m.p. 165.5–166°; $\lambda_{max}$ 230 m$\mu$ ($\epsilon$ 1.27 $\times$ $10^4$), 319 (1.77 $\times$ $10^4$); C—F stretching: 8.05 $\mu$, 8.18 $\mu$.

*Anal.* Calcd. for $C_{13}H_7F_2NO_2$: C, 63.16; H, 2.85; N, 5.67. Found: C, 63.44; H, 3.24; N, 5.63.

*1,7-Difluoro-2-fluorenamine.* The foregoing compound was reduced[10] in quantitative yield, m.p. 124–125°. One recrystallization from alcohol gave an analytical sample, m.p. 125–125.5°; $\lambda_{max}$ 287 m$\mu$ ($\epsilon$ 2.58 $\times$ $10^4$); C–F stretching: 8.1 $\mu$, 8.21 $\mu$.

*Anal.* Calcd. for $C_{13}H_9F_2N$: N, 6.45. Found: N, 6.48.

*N-2-(1,7-Difluorofluorenyl)acetamide.* Acetylation in benzene with acetic anhydride gave a quantitative yield, m.p. 198–199°. One recrystallization from alcohol (Darco) gave an analytical sample, m.p. 199–199.5°; $\lambda_{max}$ 275 m$\mu$ ($\epsilon$ 3.17 $\times$ $10^4$), 285 (3.00 $\times$ $10^4$), $\lambda_{shoulder}$ 298 m$\mu$; C—F stretching: 8.08 $\mu$, 8.29 $\mu$.

Anal. Calcd. for $C_{15}H_{11}F_2NO$: C, 69.49; H, 4.28; F, 14.66; N, 5.40. Found: C, 69.59; H, 4.32; F, 14.63; N, 5.50.

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[CONTRIBUTION FROM THE CHEMISTRY RESEARCH LABORATORY OF THE DEPARTMENT OF SURGERY, UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE]

# Derivatives of Fluorene. XVI. *N*-9-Fluorenylmaleamic Acids and Maleimides[1]

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*Received November 7, 1960*

Several *N*-9-fluorenylmaleamic acids, maleimides, and some new intermediates are described. Cyclization of three *N*-9-fluorenylmaleamic acids is effected in boiling glacial acetic acid. Acetic anhydride with fused sodium acetate, in the usual cyclization procedure, gives highly colored mixtures.

In a recent paper we described the preparation of a number of *N*-(ring)-fluorenylmaleamic acids and maleimides.[3] The end- products described below are *N*-aralkylmaleimides. Various substituents on the rings might be expected, among other effects,

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(1) Supported in part by a research grant (C-1744) from the National Cancer Institute, National Institutes of Health.

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(3) T. L. Fletcher and H. L. Pan, "Derivatives of Fluorene. XIV," submitted for publication.

to alter susceptibility to RS-H saturation of the carbon-carbon double bond. These compounds are being tested elsewhere for various biological properties including tumor inhibition screening.

In this study several *N*-9-fluorenylmaleamic acids and maleimides were synthesized, starting with 9-fluorenamine prepared by zinc dust reduction of fluorenone oxime.[4] Trifluoroacetylation gave a high yield of *N*-9-fluorenyltrifluoroacetamide. Schmidt and Stützel[5] reported that nitration of *N*-9-fluorenylacetamide in boiling nitric acid gave 1,8-dinitrofluorenone, and Bennett and Noyes[6] nitrated the same compound by means of nitric and sulfuric acid mixture obtaining a compound designated as 1,8-dinitro-9-acetamidofluorene. However, *N*-9-fluorenyltrifluoroacetamide when nitrated under mild conditions gave good yields of *N*-9-(2-nitrofluorenyl)trifluoroacetamide. The position of the nitro group was established by dichromate oxidation to 2-nitrofluorenone.

Acid hydrolysis of *N*-9-(2-nitrofluorenyl)trifluoroacetamide gave 2-nitro-9-fluorenamine. Reaction of the latter with maleic anhydride gave *N*-9-(2-nitrofluorenyl)maleamic acid which was cyclized to the corresponding maleimide in boiling glacial acetic acid. Attempts to close the maleamic acid, in acetic anhydride in the presence of fused sodium acetate, led to a dark purple solid which could not be purified by crystallization or by chromatography on alumina.

Reduction[7] of 2-nitro-9-trifluoroacetamidofluorene gave the 2-amine which was acetylated. The latter compound was hydrolyzed by brief boiling in dilute sodium hydroxide solution giving 2-acetamido-9-fluorenamine, an unstable compound. This amine was also obtained by zinc dust–acetic acid reduction of 2-acetamidofluorenone oxime. In neither case were we able to prepare an analytical sample. However, upon crystallization from acetone, *N*-2-(9-isopropylidenaminofluorenyl)acetamide was obtained as shown by microanalyses and infrared spectrum.

The above amine reacted with maleic anhydride giving an almost quantitative yield of *N*-9-(2-acetamidofluorenyl)maleamic acid. Attempted cyclization in acetic anhydride with fused sodium acetate led to a purple solid which decomposed upon attempted purification. Closure was effected by prolonged refluxing in glacial acetic acid with anhydrous sodium acetate. In addition to the maleimide, a high-melting white solid was obtained.

*N*-9-Fluorenylmaleamic acid, prepared from the 9-amine, also gave a dark purple intractable solid when heated in acetic anhydride with fused sodium acetate. The corresponding maleimide was obtained by refluxing a mixture of 9-fluorenamine, maleic anhydride, and anhydrous sodium acetate in glacial acetic acid. This maleimide gave an addition compound when treated with *N*-2-(α-thiolnaphthyl)acetamide.

9-Trifluoroacetamido-2-fluorenamine gave *N*-2-(9-trifluoroacetamidofluorenyl)maleamic acid, which cyclized in the acetic anhydride procedure. Upon alkaline hydrolysis, this maleamic acid gave the supposed *N*-2-(9-aminofluorenyl)maleamic acid (not characterized) which was treated with acetic anhydride and sodium acetate. A yellow crystalline solid resulted which was not the expected 9-acetamidomaleimide. Further characterization has not been attempted.

Attempts to prepare 2,9-dimaleimidofluorene from 2,9-diaminofluorene[6] were not successful. With an excess or an equivalent amount of maleic anhydride, the diamine gave a compound of unknown structure.

## EXPERIMENTAL[8]

*N-9-Fluorenyltrifluoroacetamide.* To a cooled (10°) mixture of 9-aminofluorene hydrochloride (21.8 g., 0.1 mole) and pyridine (80 ml.), trifluoroacetic anhydride (23.1 g., 0.11 mole) was added with stirring over a period of 5 min. The reaction mixture was allowed to stand at room temperature for 0.5 hr. then heated on a steam bath for 0.25 hr. and cooled. After water dilution the precipitated product weighed 23.9 g. (87%), m.p. 251–252.5°. Recrystallization from methanol gave an analytical sample, m.p. 252–253° (preheated block). $\lambda_{max}^{C_2H_5OH}$ : 224 mμ (log ε 4.40), 232 (4.24), 268 (4.34), 292 (3.80), 304 (3.59). $\nu_{N-H}$ 3290, 1550; $\nu_{C=O}$ 1700; $\nu_{C-F}$ 1180 cm.$^{-1}$ (broad).

*Anal.* Calcd. for $C_{15}H_{10}F_3NO$: C, 64.98; H, 3.64; N, 5.05. Found: C, 65.34; H, 3.69; N, 4.85.

*N-9-(2-Nitrofluorenyl)trifluoroacetamide.* A mixture of nitric acid (*d.* 1.42) (0.7 ml., ~ 0.011 mole) and glacial acetic acid (1.5 ml.) was added portionwise (10 min.) to a stirred suspension of *N*-9-fluorenyltrifluoroacetamide (1.9 g., 0.007 mole) in glacial acetic acid (15 ml.) and concd. sulfuric acid (1 ml.) at 75°. The temperature was kept at 75–80° for 5 min., with stirring, and then allowed to drop to room temperature. After water dilution and filtration the crude product, 2.2 g. (98%), was recrystallized from methanol-benzene giving 1.6 g. (71%), m.p. 234.5–235.5°. Further crystallization gave an analytical sample, m.p. 236–237°. $\nu_{N-H}$ 3300, 1550; $\nu_{C=O}$ 1710; $\nu_{NO_2}$ 1345; $\nu_{C-F}$ 1180 cm.$^{-1}$ (broad).

*Anal.* Calcd. for $C_{15}H_9F_3N_2O_3$: C, 55.91; H, 2.82; N, 8.69. Found: C, 55.96; H, 2.83; N, 8.78.

*Oxidation of N-9-(2-nitrofluorenyl)trifluoroacetamide.* A mixture of the trifluoroacetamide (0.1 g.), potassium dichromate (0.3 g.), 9*N* sulfuric acid (4 ml.), and glacial acetic acid (4 ml.) was refluxed for 1 hr. and the reaction mixture then diluted with water. There was obtained 0.05 g. (70%)

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(4) C. K. Ingold and C. L. Wilson, *J. Chem. Soc.*, 1493 (1933).

(5) J. Schmidt and H. Stützel, *Ann.*, **370**, 1 (1909).

(6) C. W. Bennett and W. A. Noyes, *J. Am. Chem. Soc.*, **52**, 3437 (1930).

(7) T. L. Fletcher and M. J. Namkung, *J. Org. Chem.*, **23**, 680 (1958).

(8) Melting points were taken on a Fisher-Johns block and are corrected to standards. The analyses were done by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.; A. Bernhardt, Mülheim (Ruhr); and W. Manser, Zürich. The ultraviolet absorptions were measured with a Beckman DK-1 Recording Spectrophotometer. The solutions had been prepared immediately before the measurements were made. The infrared spectra were run on a Beckman IR-5 (potassium bromide disk).

of 2-nitrofluorenone, m.p. and mixture m.p. 225–226°. The infrared spectrum of this substance was identical with that of authentic 2-nitrofluorenone.

*Acid hydrolysis of N-9-(2-nitrofluorenyl)trifluoroacetamide.* The amide (2 g., 0.006 mole) was refluxed for 9 hr. in a mixture of concd. hydrochloric acid (8 ml.) and absolute ethanol (50 ml.) and the solvent was distilled under reduced pressure until crystallization of the amine hydrochloride took place. This was filtered, washed with 6*N* hydrochloric acid, and dried giving 1.55 g. (96%). The product started melting with decomposition at 206°, but no definite melting point was observed.

*N-9-(2-Nitrofluorenyl)maleamic acid.* A suspension of 2-nitro-9-fluorenamine hydrochloride (0.5 g., 0.002 mole) in glacial acetic acid (20 ml.) and anhydrous sodium acetate (0.2 g., 0.002 mole) was heated until most of the amine hydrochloride went into solution. The hot mixture was then added in one portion to a rapidly stirred solution of maleic anhydride (0.3 g., 0.003 mole) in glacial acetic acid (5 ml.). After 30 min. of stirring the reaction mixture was set aside for 1 hr. then diluted with water. The product 0.55 g. (90%), melted (dec.) at 203–205°. Crystallization from acetone gave an analytical sample, m.p. 208.5–209.5° dec. $\lambda_{max}^{C_2H_5OH}$: 329 mμ (log ε 4.23). $\nu_{N-H}$ 3250, 1550; $\nu_{C=O}$ 1710; $\nu_{NO_2}$ 1340 cm.$^{-1}$

*Anal.* Calcd. for $C_{17}H_{12}N_2O_5$: C, 62.96; H, 3.73; N, 8.64. Found: C, 63.30; H, 3.77; N, 8.80.

*N-9-(2-Nitrofluorenyl)maleimide.* (a) A mixture of *N*-9-(2-nitrofluorenyl)maleamic acid (0.5 g.), fused sodium acetate (0.1 g.), and acetic anhydride (5 ml.) was heated on a steam bath for 15 min. with frequent shaking. The deep purple reaction solution was treated with dilute sodium carbonate and a resinous solid (0.5 g.) was obtained. Attempts to purify this solid, both by crystallization and chromatography on alumina, were unsuccessful.

(b) *N*-9-(2-Nitrofluorenyl)maleamic acid (0.5 g.) was refluxed in glacial acetic acid (25 ml.) under an air condenser for 7 hr. and the solvent distilled. The residual oil solidified upon cooling and was recrystallized from 95% ethanol giving 0.33 g., m.p. 218–223°. Further crystallization from ethanol gave an analytical sample, m.p. 242.5–243.5°. $\lambda_{max}^{C_2H_5OH}$: 328 mμ (log ε 4.25). $\nu_{C=O}$ 1715; $\nu_{NO_2}$ 1340 cm.$^{-1}$

*Anal.* Calcd. for $C_{17}H_{10}N_2O_4$: C, 66.66; H, 3.29; N, 9.15. Found: C, 66.54; H, 3.59; N, 9.10.

*N-9-(2-Aminofluorenyl)trifluoroacetamide.* *N*-9-(2-Nitrofluorenyl)trifluoroacetamide (3 g.) was reduced[7] in boiling 95% ethanol (150 ml.) with hydrazine hydrate (100%), (1.5 ml.) and Raney nickel, giving 2.6 g. (97%) of the amine, m.p. 267–268°.

*N-Acetyl derivative:* m.p. 297.5–299° dec. $\lambda_{max}^{C_2H_5OH}$: 224 mμ (log ε 4.56), 238 (shoulder), 293 (4.43), 304 (shoulder). $\nu_{N-H}$ 3270, 1550; $\nu_{C=O}$ 1710, 1665; $\nu_{C-F}$ 1190 cm.$^{-1}$ (broad).

*Anal.* Calcd. for $C_{17}H_{13}F_3N_2O_2$: C, 61.08; H, 3.92; N, 8.38. Found: C, 61.20; H, 4.19; N, 8.19.

Hydrolysis of the latter derivative (0.1 g.) by boiling for 1 min. in a mixture of 95% ethanol (1 ml.) and 2% sodium hydroxide (4 ml.) gave 2-acetamido-9-fluorenamine identical with the compound prepared by reduction of 2-acetamidofluorenone oxime. Recrystallization of this amine from acetone gave the azomethine, described below, obtained from the recrystallization of the reduction product of 2-acetamidofluorenone oxime.

*2-Acetamidofluorenone oxime.* A mixture of hydroxylamine hydrochloride (9 g., 0.13 mole) and anhydrous sodium acetate (13.1 g., 0.16 mole) was dissolved in water (40 ml.). To the solution 2-acetamidofluorenone (15.8 g., 0.07 mole) and ethanol (100 ml.) were added with stirring. The whole was then refluxed for 10 min., cooled, diluted with water, and the product filtered, giving 15.3 g. (92%), m.p. 237–238.5° dec.

Recrystallization from methanol gave an analytical sample, m.p. 238–239° dec.

*Anal.* Calcd. for $C_{15}H_{12}N_2O_2 \cdot CH_3OH$: C, 67.60; H, 5.67; N, 9.86. Found: C, 68.14; H, 5.76; N, 10.26.

*N-2-(9-Aminofluorenyl)acetamide.* Reduction of the oxime (2 g.) in acetic acid–water (12:1) (13 ml.) with zinc dust (2.6 g.) at 90–95° (bath) (20 min.) gave 1.9 g. (quant.), m.p. 160–163° dec.

Recrystallization from acetone gave *N-2-(9-isopropylidenaminofluorenyl)acetamide*, m.p. 209–211° dec. The infrared spectrum (potassium bromide disk, cm.$^{-1}$) showed no absorption corresponding to a primary amino group but intense absorption at 2970, 2870 ($CH_3$); 1680 (C=N); and 1665 (C=O of the acetamido group). $\lambda_{max}^{C_2H_5OH}$: 213 mμ (shoulder), 236 (shoulder), 282 (shoulder), 291 (log ε 4.52), 306 (shoulder).

*Anal.* Calcd. for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.07. Found: C, 77.82; H, 6.86; N, 10.06.

*N-9-(2-Acetamidofluorenyl)maleamic acid.* To a stirred solution of maleic anhydride (3 g., 0.03 mole) in glacial acetic acid (20 ml.), *N*-2-(9-aminofluorenyl)acetamide (6.8 g., 0.03 mole) in glacial acetic acid (60 ml.) was added over a period of 20 min. The resulting thin paste was stirred for 2 hr. then filtered. The product was washed with acetic acid and dried on the funnel giving 8.7 g. (95%), m.p. 209.5–212° dec. Recrystallization from acetone gave an analytical sample, m.p. 213–214° dec. $\lambda_{max}^{C_2H_5OH}$: 214 mμ (log ε 4.63), 238 (shoulder), 282 (shoulder), 292 (4.48), 307 (shoulder). $\nu_{N-H}$ 3280, 1550; $\nu_{C=O}$ 1710, 1667 cm.$^{-1}$

*Anal.* Calcd. for $C_{19}H_{16}N_2O_4$: C, 67.85; H, 4.80; N, 8.33. Found: C, 67.70; H, 4.82; N, 8.44.

*N-9-(2-Acetamidofluorenyl)maleimide.* The foregoing maleamic acid (2 g.) was refluxed 22 hr. in glacial acetic acid (50 ml.) with anhydrous sodium acetate (2 g.). The excess solvent was distilled and the residual solid triturated in ice water, filtered, and washed with water. When dry the solid was extracted with boiling benzene and the extract evaporated to an oily solid which was crystallized from acetone. A small amount of white solid (m.p. > 280°) of unknown composition was removed. The first crop was recrystallized successively from acetone-water, benzene-cyclohexane (twice), and benzene (twice) giving yellowish white prisms, 0.2 g., m.p. 221–223°. $\lambda_{max}^{C_2H_5OH}$: 237 mμ (shoulder), 281 (log ε 4.64), 291 (4.62). $\nu_{N-H}$ 3390, 1540; $\nu_{C=O}$ 1705, 1670 cm.$^{-1}$

*Anal.* Calcd. for $C_{19}H_{14}N_2O_3$: C, 71.69; H, 4.43; N, 8.80. Found: C, 71.83; H, 4.59; N, 8.80.

*N-9-Fluorenylmaleamic acid.* 9-Aminofluorene (9.05 g., 0.05 mole) was dissolved in warm glacial acetic acid (40 ml.) and added slowly (15 min.) to a stirred solution of maleic anhydride (5.5 g., 0.055 mole) in glacial acetic acid (20 ml.). After a half hour of stirring the reaction mixture was heated on a steam bath for 15 min. and cooled. Upon water dilution there was obtained 13.6 g. (98%) of the maleamic acid, m.p. 201–203.5° dec. (preheated block). $\lambda_{max}^{C_2H_5OH}$: 224 mμ (log ε 4.49), 232 (4.33), 268 (4.33), 292 (3.77), 304 (3.62). $\nu_{N-H}$ 3260, 1540; $\nu_{C=O}$ 1700 cm.$^{-1}$

*Anal.* Calcd. for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.28; H, 4.99; N, 4.72.

*N-9-Fluorenylmaleimide.* Maleic anhydride (1.1 g., 0.011 mole) was added to a mixture of 9-aminofluorene hydrochloride (2.18 g., 0.01 mole; Aldrich Chemical Co., Milwaukee, Wis.), glacial acetic acid (23 ml.), and anhydrous sodium acetate (0.9 g., 0.011 mole). The whole was shaken and refluxed under an air condenser for 2 hr. and cooled. After water dilution the gummy solid was recrystallized from methanol-water and from benzene-ligroin (*d.* 0.67–0.69). A small amount of the maleamic acid was first removed by filtration. Evaporation of solvent gave a second crop which was recrystallized from methanol-water giving lustrous white needles (0.2 g.), m.p. 171–173°. Further crystallization from the same solvent gave an analytical sample, m.p. 174–175°. $\lambda_{max}^{C_2H_5OH}$: 224 mμ (log ε 4.51), 232 (4.34), 268 (4.28), 279 (shoulder), 293 (3.73), 304 (3.62). The ultraviolet absorption in cyclohexane was quite similar. $\nu_{C=O}$ 1700 cm.$^{-1}$

*Anal.* Calcd. for $C_{17}H_{11}NO_2$: C, 78.15; H, 4.24; N, 5.36. Found: C, 78.19; H, 4.34; N, 5.55.

*N-9-Fluorenyl-α-S-[1′-(2′-acetamidonaphthyl)]mercapto-*

*succinimide.* The foregoing maleimide (0.05 g.) was dissolved in acetone (3 ml.). To the solution *N*-2-($\alpha$-thiolnaphthyl)-acetamide (1.1 equivalents) in acetone (3 ml.) was added dropwise (5 min.). The reaction solution was stirred for 20 min. and concentrated to an oil. Methanol was added to the oil and the mixture was concentrated until crystallization of a white substance took place. After filtration and recrystallization from acetone-methanol, 0.08 g., m.p. 208–209° was obtained. Two recrystallizations from acetone-water gave an analytical sample, m.p. 211–212°.

*Anal.* Calcd. for $C_{29}H_{22}N_2O_3S$: N, 5.85; S, 6.70. Found: N, 5.83; S, 6.56.

*N-2-(9-Trifluoroacetamidofluorenyl)maleamic acid.* *N*-9-(2-Aminofluorenyl)trifluoroacetamide (0.2 g., 0.7 mmole) reacted with maleic anhydride (0.14 g., 1.4 mmoles) in glacial acetic acid (10 ml.) giving a quantitative yield (0.27 g.) of the maleamic acid, m.p. 223–225° dec. An analytical sample was prepared by stirring the product with boiling acetone and filtering, m.p. 225–227° dec. $\lambda_{max}^{C_2H_5OH}$: 276 m$\mu$ (log $\epsilon$ 4.14), 319 (4.22). $\nu_{N-H}$ 3310, 1550; $\nu_{C=O}$ 1710; $\nu_{C-F}$ 1175 cm.$^{-1}$ (broad).

*Anal.* Calcd. for $C_{19}H_{13}F_3N_2O_4$: C, 58.47; H, 3.36; N, 7.18. Found: C, 58.54; H, 3.63; N, 714.

*N-2-(9-Trifluoroacetamidofluorenyl)maleimide.* The above maleamic acid (7.8 g.) was cyclized in acetic anhydride (30 ml.), in the presence of fused sodium acetate (1.2 g.), giving 7.1 g. (96%) of the maleimide, m.p. 255–259°. Recrystallization from benzene gave an analytical sample, m p. 262–263°. $\lambda_{max}^{C_2H_5OH}$ 234 m$\mu$ (shoulder), 277 (log $\epsilon$ 4.36), 306 (3.83). $\nu_{N-H}$ 3330, 1550; $\nu_{C=O}$ 1730, 1710; $\nu_{C-F}$ 1180 cm.$^{-1}$ (broad).

*Anal.* Calcd. for $C_{19}H_{11}F_3N_2O_3$: C, 61.30; H, 2.98; N, 7.53. Found: C, 61.44; H, 2.98; N, 7.78.

*Attempted preparation of N-2-(9-acetamidofluorenyl)-maleimide.* *N*-2-(9-Trifluoroacetamidofluorenyl)maleamic acid (4 g.) was dissolved in 1*N* sodium hydroxide (50 ml.), heated on a steam bath for 3 min., and cooled. A small amount of fluffy precipitate was removed. The alkaline solution was chilled in ice and acidified to *p*H 4 with hydrochloric acid. The yellow precipitate was filtered, washed once with ice water, and dried giving 3.3 g., m.p. 185–190° dec.

The latter compound (1 g.) was mixed with fused sodium acetate (0.15 g.) and acetic anhydride (6 ml.) and heated on a steam bath, with shaking, for 15 min. and cooled to room temperature. The pasty mixture was stirred in 10% sodium acetate and the excess acetic anhydride destroyed with 5% sodium carbonate. The yellow solid was filtered, washed with water, and dried, giving 0.9 g. Recrystallization from acetone-benzene-ligroin gave 0.85 g., m.p. 190–192° dec. Three recrystallizations from acetone-water gave an analytical sample, m.p. 209–211° (glassy).

*Anal.* Found: C, 69.19; H, 5.09; N, 8.86.

*Attempted preparation of N,N′-2,9-fluorenedimaleamic acid.* 2,9-Diaminofluorene[6] (1.96 g., 0.01 mole) in warm glacial acetic acid (10 ml.) was added dropwise to a warm solution of maleic anhydride (2.94 g., 0.03 mole) in glacial acetic acid (15 ml.) over a period of 20 min. The reaction mixture was stirred at room temperature for 30 min. then heated (steam bath) for 10 min. and cooled. Water dilution of the mixture gave 3.8 g. (97.5%) of an acidic substance, m.p. ~ 212° dec.

Recrystallization from acetone-methanol gave a sample, m.p. 210–211° dec. (preheated block).

*Anal.* Found: C, 61.44; H, 4.91; N, 5.68.

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[CONTRIBUTION NO. 304 FROM THE JACKSON LABORATORY, ORGANIC CHEMICALS DEPARTMENT,
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# *m*-Dioxanes and Other Cyclic Acetals

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*Received November 10, 1960*

An extensive series of substituted *m*-dioxanes has been prepared by acetalization of 1,3-glycols. Some 1,3-dioxolanes, 1,3-oxathianes, and 1,3-dioxolanes have been synthesized for comparison. Differences in the ease of acetalization have been noted.

The study of catalytic reactions of *m*-dioxanes[1] required the preparation of a variety of *m*-dioxanes and related acetals. Although the basic synthetic method, direct acid-catalyzed reaction of 1,3-diols (or in a few cases, 1,2- or 1,4-diols) with aldehydes or ketones has long been known, it was necessary to develop refinements of this procedure to obtain satisfactory yields of certain acetals.

Some unstable aldehydes—*e.g.*, chloroacetaldehyde and malonaldehyde—are marketed as their methyl or ethyl acetals. These were conveniently converted to the *m*-dioxanes by interchange with the diol in the presence of boron trifluoride or *p*-toluenesulfonic acid. The lower alcohol was distilled during the interchange to shift the equilibrium.

Although quantitative kinetic experiments were not performed, the qualitative effects of substituents on the rate and equilibria were noted. The aromatic aldehydes reacted very rapidly, with simple aliphatic aldehydes next in line. Ketones seemed to react rapidly, but the equilibrium position was less favorable. With acetone, very little product was formed (infrared) until the water was removed from the distillate by drying it with calcium chloride. It was surprising to find that the cyclopentanone ketal (#11)[2] was hydrolyzed rapidly by distilled water, in which the dissolved carbon dioxide must function as the acid catalyst. This was not the case with the acetone (#10) and cyclohexanone (#12) ketals. These results are in line with the prediction from the I-strain principle,[3] which teaches that reactions in which a ring carbon atom changes from

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[1] C. S. Rondestvedt, Jr., and G. J. Mantell, *J. Am. Chem. Soc.*, **82**, 6419 (1960).

[2] The arabic numerals are those assigned to the acetals in the tables.

[3] H. C. Brown, R. S. Fletcher, and R. B. Johannessen, *J. Am. Chem. Soc.*, **73**, 212 (1951).