separated and was collected after cooling at 0° for about two hours. A solution of the product in benzene was passed through a column of activated alumina and Super-Cel. No fluorescence was observed under ultraviolet light, but a dark brown layer of impurities was left at the top of the column and the principal zone was yellow and could be eluted readily with benzene. After complete removal of the benzene by evaporation, the residue was crystallized from a small volume of ether and gave 0.42 g. (34%) of small, yellow, microcrystalline clusters, m. p. 114–117°. The compound crystallizes much better from absolute alcohol, and after two more recrystallizations from this solvent it formed pale yellow plates, m. p. 118–118.5°. The pure substance shows a yellow fluorescence in ultraviolet light.

Anal. Calcd. for $C_{18}H_{14}Se$: C, 69.90; H, 4.56. Found: C, 69.98; H, 4.86.

The **picrate** forms dark brown needles from absolute alcohol, m. p. 145.5–146°.

Anal. Calcd. for $C_{18}H_{14}Se \cdot C_6H_3O_7N_3$: N, 7.81. Found: N, 7.75.

The **trinitrobenzene derivative** forms maroon-colored needles from absolute alcohol and melts at 173.5–174°.

Anal. Calcd. for $C_{18}H_{14}Se \cdot C_6H_3O_6N_3$: N, 8.05. Found: N, 8.17.

Summary

Syntheses are reported for isologs of 9,10-dimethyl-1,2-benzanthracene in which the 1,2-benz ring is replaced by a thiophene and by a selenophene ring.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASS. RECEIVED JULY 8, 1941

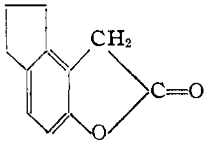
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF TRINITY COLLEGE]

Fluorenone-2,3-dicarboxylic Acid and its Anhydride

BY WARREN C. LOTHROP AND JOHN A. COFFMAN

It has recently been suggested[1] that fluorenone-2,3-dicarboxylic anhydride would be of interest as an analog of phthalic acid. Moreover, the compound seemed of value to us as a test case involving the Mills–Nixon effect, inasmuch as it contains two five-membered rings on opposite sides of a benzene ring. Such an arrangement would impose some strain on one of these rings which would very likely manifest itself in some instability of the anhydride ring, although it is not to be anticipated from previous work[2] that this strain would be very great.

Examples of similar compounds are few and ambiguous. While pyromellitic acid readily forms a di-anhydride and a di-imide, indicating no strain, a case more comparable with our own has recently been reported[3] where a Mills–Nixon strain is apparently operative: the formation of lactones I and II from the corresponding hydroxy acids proceeding in the former case spontaneously but in the latter only upon heating with concentrated sulfuric acid.



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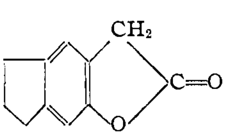
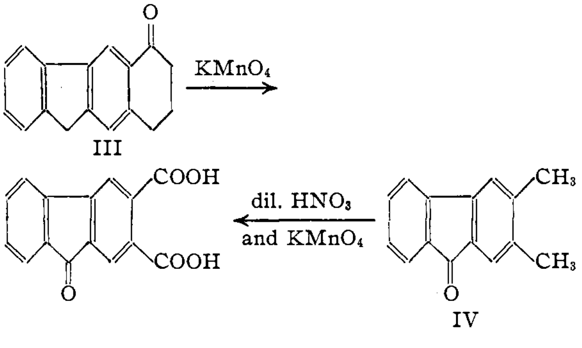


II

The preparation of the desired dicarboxylic acid was found to involve considerable difficulty although it was finally achieved by two independent methods, using oxidations of ketotetrahydrobenzofluorene (III) and of 2,3-dimethylfluorenone (IV)



The first method proved unsatisfactory only because of the last step, since the previously prepared[4] compound III was readily obtained in good yield by ring closure of γ-2-fluorylbutyric acid with anhydrous hydrogen fluoride. Oxidation of III by various reagents (dilute nitric acid, potassium dichromate in acetic acid, potassium permanganate in acid solution or in acetone, and selenium dioxide in dioxane) gave resins or unreacted material. Only alkaline permanganate

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[1] Rieveschl and Ray, *Chem. Rev.*, **23**, 365 (1938); but see Dziewonski, Kuzdrzal and Mayer, *Bull. Acad. Polonaise*, **348A** (1934), regarding failure to obtain 2,3-diacetylfluorene, the most likely starting material.

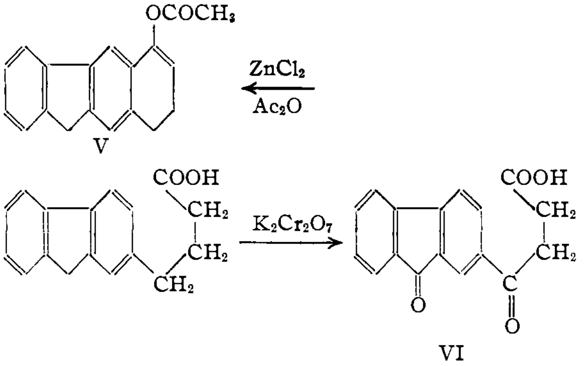
[2] Lothrop, THIS JOURNAL, **61**, 2115 (1939).

[3] Arventi, *Ann. sci. univ. Jassy*, Pt. I, **25**, 692 (1939).

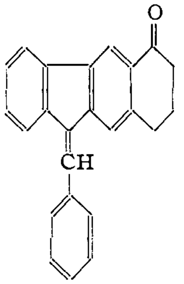
[4] Koelsch, THIS JOURNAL, **55**, 3885 (1933).

succeeded and even then the best yield of twenty experiments was but 13%.

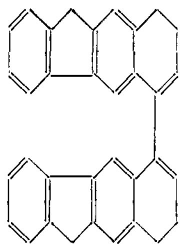
Various attempted alterations of III were equally fruitless. When ring closure of γ-2-fluorylbutyric acid by the action of zinc chloride and acetic anhydride[5] was attempted the product was the corresponding anhydride rather than the desired enol acetate V, while an attempt to prepare γ-2-fluorenone-butyric acid by oxidizing the apparently troublesome methylene group at position 9 gave instead β-2-fluorenonoylpropionic acid[4] VI which could not be reduced by the Clemmensen procedure.



Condensation of the active methylene group with benzaldehyde was readily accomplished but the product VII as well as the diene product VIII of pinacol reduction[6] and dehydration could not be oxidized satisfactorily.



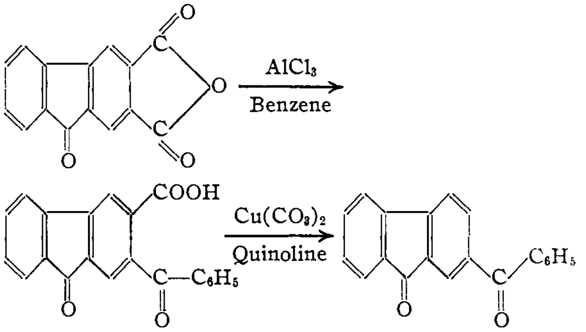
VII



VIII

The second and more orthodox method of preparation using the Ullmann reaction gave 2,3-dimethylfluorenone IV in excellent yield from *o*-xylene. Oxidation of this by dilute nitric acid formed 3-methylfluorenone-2-carboxylic acid which was further oxidized by alkaline permanganate to the identical dicarboxylic acid prepared by the first method, but in much better yield.

When fluorenone-2,3-dicarboxylic acid was refluxed with acetic anhydride the anhydride formed without difficulty. It entered into a Friedel–Crafts reaction with benzene yielding 2-benzoylfluorenone-3-carboxylic acid as was proved by decarboxylation of the latter to 2-benzoylfluorenone and comparison with an authentic sample



The anhydride was hydrolyzed by sodium bicarbonate at a rate comparable with phthalic anhydride, formed an anil, and gave on fusion with phenol and resorcinol products similar to phenolphthalein and fluorescein but exhibiting deeper color changes and enhanced fluorescence. In fact no evidence could be found that the Mills–Nixon effect was operating to cause any strain in the anhydride ring, or that any unusual difference existed between phthalic anhydride and its analog.

Unfortunately fluorene-2,3-dicarboxylic acid and its anhydride could not be prepared since red phosphorus with hydriodic acid and sodium amalgam[7] both failed to reduce the fluorenone dicarboxylic acid or its anhydride.

Experimental Part

β-3-Fluoroylpropionic acid was found in the mother liquors from the recrystallization of crude **β-2-fluoroylpropionic acid** described by Koelsch.[4] It represented 2–3% of the total yield and was recovered by crystallizations from 50% acetic acid and from 50% alcohol as white prisms m. p. 162–164°.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.67; H, 5.30. Found: C, 76.41; H, 5.51.

β-3-Fluorenonoylpropionic acid resulted on oxidation of the fluoroylpropionic acid with a refluxing solution of sodium dichromate in glacial acetic acid. It crystallized from alcohol in fine, yellow needles (m. p. 178–180° dec.) in 60% yield. *Anal.* Calcd. for $C_{17}H_{12}O_4$: C, 72.84; H, 4.32. Found: C, 72.70; H, 4.52. Alkaline permanganate oxidation of the above acid gave a fluorenone carboxylic acid crystallizing from glacial acetic acid in yellow needles, m. p. 284–285°. This corresponds with the reported m. p. of the 3 acid[8] (285–286°), the 1 and 2 isomers melting at 245 and 338°, respectively.

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(5) Fieser and Hershberg, THIS JOURNAL, **59**, 1028 (1937).

(6) Newman, *ibid.*, **62**, 1683 (1940).

(7) Fieser and Seligman, *ibid.*, **57**, 2174 (1935).

(8) Sieglitz and Schatzkes, *Ber.*, **54**, 2070 (1921).

γ-2-Fluorylbutyric acid was prepared according to Koelsch[4] and ring closed by the action of ten times its weight of anhydrous hydrogen fluoride at 0°. The alkali-insoluble material was crystallized from alcohol in small, white plates m. p. 149–150° in 91% yield. This compares with a 75% yield of **ketotetrahydrobenzofluorene** III obtained by the internal Friedel–Crafts procedure.

Fluorenone-2,3-dicarboxylic Acid.—To a well-stirred suspension of 5 g. of III in 300 cc. of 2% sodium hydroxide at 80–90°, powdered potassium permanganate (24 g.) was added over a period of two hours. After three hours of further heating and stirring, the manganese dioxide was filtered off and from it on treatment with sulfur dioxide 1.3 g. of unchanged material was recovered. The alkaline filtrate on acidification gave a product crystallizing from glacial acetic acid in tiny, bright yellow rosets. It melted with loss of water at 250–275° and weighed 0.5 g. (13% yield) while on distillation it yielded fluorenone. *Anal.* Calcd. for $C_{15}H_8O_5$: C, 67.19; H, 3.01. Found: C, 66.78; H, 3.28.

Its dimethyl **ester** crystallized from methanol in long yellow needles, m. p. 131–133°. *Anal.* Calcd. for $C_{17}H_{12}O_5$: C, 68.90; H, 4.08. Found: C, 68.88; H, 4.29.

Its **diethyl ester** crystallized from ethanol in yellow needles, m. p. 161–162°. *Anal.* Calcd. for $C_{19}H_{16}O_5$: C, 70.36; H, 4.97. Found: C, 70.09; H, 4.90.

γ-2-Fluorylbutyric anhydride resulted when 10 g. of the corresponding acid in 60 cc. of glacial acetic acid and 40 cc. of acetic anhydride was refluxed with 1 g. of powdered anhydrous zinc chloride.[5] It crystallized from acetic acid in very small prisms, m. p. 132–133°. *Anal.* Calcd. for $C_{34}H_{30}O_3$: C, 83.92; H, 6.23. Found: C, 83.90; H, 6.41. When the above anhydride was treated with concentrated ammonia or when the free acid was refluxed with thionyl chloride and then heated with ammonia, **γ-2-fluorylbutyramide** resulted; white plates from alcohol, m. p. 192–193°. *Anal.* Calcd. for $C_{17}H_{17}ON$: N, 5.58. Found: N, 5.58.

11-Benzal-ketotetrahydrobenzofluorene VII.—To a solution of 3 g. of sodium in 150 cc. of absolute alcohol, 5 g. of III and 4 g. of benzaldehyde were added. The solution was allowed to stand overnight at 65° and the product which separated crystallized from glacial acetic acid in bright yellow needles. It weighed 5.8 g. (84%) and melted at 234–235°. *Anal.* Calcd. for $C_{24}H_{18}O$: C, 89.40; H, 5.63. Found: C, 89.69; H, 5.95.

8,9,8′,9′-Tetrahydro-6,6′-bibenzofluoryl VIII was prepared following Newman's procedure.[6] As in his work the pinacol was not purified but was dehydrated immediately by the action of boiling acetic acid. After two recrystallizations from glacial acetic acid the product was obtained in white needles, m. p. 193–195°. The yield was 3.1 g. or 67%. *Anal.* Calcd. for $C_{34}H_{26}$: C, 93.96; H, 6.03. Found: C, 93.55; H, 5.66.

3,4-Dimethyl-2′-(4-toluenesulfonamido)-benzophenone was formed in 62% yield in the usual way[2] from *o*-xylene and 2-(4-toluenesulfonamido)-benzoyl chloride. It crystallized in small, white prisms, m. p. 132–133°. *Anal.* Calcd. for $C_{22}H_{21}O_3NS$: C, 69.66; H, 5.54; N, 3.69. Found: C, 69.38; H, 5.64; N, 4.05.

Its **methyl derivative** was prepared by the action of dimethyl sulfate and crystallized from dilute alcohol in white prisms, m. p. 119–120°. *Anal.* Calcd. for $C_{23}H_{23}O_3NS$: C, 70.23; H, 5.85; N, 3.56. Found: C, 70.58; H, 6.10; N, 3.34.

3,4-Dimethyl-2′-aminobenzophenone was prepared in 90% yield by a previously employed procedure.[2] It formed pale yellow needles from methanol, m. p. 82°. *Anal.* Calcd. for $C_{15}H_{15}ON$: C, 80.00; H, 6.67; N, 6.22. Found: C, 79.89; H, 6.62; N, 5.96.

2,3-Dimethylfluorenone IV was prepared by the Ullmann reaction[2] on the above amine in 69% yield and crystallized from alcohol in bright yellow plates,[9] m. p. 107–108°.

Reduction of 1.0 g. of the fluorenone IV with 0.2 g. of red phosphorus and 7 cc. of 47% hydriodic acid in 15 cc. of glacial acetic acid, gave 0.7 g. (75%) of **2,3-dimethylfluorene** crystallizing from alcohol in fine, white prisms,[10] m. p. 124–125°.

3-Methylfluorenone-2-carboxylic acid resulted when a mixture of 6.0 g. of IV, 100 cc. of concentrated nitric acid and 400 cc. of water was refluxed for forty hours. The product crystallized from glacial acetic acid in light yellow needles m. p. 307–309° and weighed 5.1 g. (74%). *Anal.* Calcd. for $C_{15}H_{10}O_3$: C, 75.60; H, 4.25. Found: C, 75.81; H, 4.02.

Its **methyl ester** separated from methanol in light yellow rosets, m. p. 175–176°. *Anal.* Calcd. for $C_{16}H_{12}O_3$: C, 76.15; H, 4.80. Found: C, 75.97; H, 4.72. When the above acid was heated to 210° for fifteen minutes in quinoline solution with copper carbonate, decarboxylation was effected and a product crystallized from petroleum ether in long, yellow needles, m. p. 67–68°. This was evidently 3-methylfluorenone whose m. p. is reported[11] to be 66.5° while that reported[12] for 2-methylfluorenone is 92°.

When a solution of 5.4 g. of 3-methylfluorenone-2-carboxylic acid in 400 cc. of 1% sodium hydroxide at 70° was treated with 8.8 g. (15% excess) of potassium permanganate in the manner already described, 4.0 g. of **fluorenone-2,3-dicarboxylic acid** resulted—a 66% yield. **3-Methylfluorene-2-carboxylic acid** was formed by reduction of the fluorenone acid with red phosphorus and hydrogen iodide. It crystallized from glacial acetic acid in white plates, m. p. 261–263° in 85% yield. *Anal.* Calcd. for $C_{15}H_{12}O_2$: C, 80.33; H, 5.40. Found: C, 80.17; H, 5.48.

Its **methyl ester** crystallized from methanol in small, white plates, m. p. 119–120°. *Anal.* Calcd. for $C_{16}H_{14}O_2$: C, 80.63; H, 5.92. Found: C, 80.77; H, 6.27.

Fluorenone-2,3-dicarboxylic acid anhydride resulted on refluxing a mixture of 1.0 g. of the dicarboxylic acid and 35 cc. of acetic anhydride for three hours. On cooling, the product separated as yellow needles, m. p. 322–323°, weighing 0.77 g. (83%). *Anal.* Calcd. for $C_{15}H_6O_4$: C, 72.02; H, 2.40. Found: C, 72.25; H, 2.49.

An exact quantitative determination of the rate of hydrolysis seemed beyond the scope of the present work,[13] but two runs were made in which equal mole fractions of phthalic anhydride and the fluorenone anhydride were

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[9] Fujise, *ibid.*, **71**, 2461 (1938), reports 109–110°.

[10] Alder and Rickert, *ibid.*, **71**, 379 (1938), report 125–126° by a different procedure.

[11] Ullmann and Mallet, *ibid.*, **31**, 1694 (1898).

[12] Kruber, *ibid.*, **65**, 1382 (1932).

[13] *Cf.* Rivett and Sidgwick, *J. Chem. Soc.*, **97**, 1677 (1910).

shaken at room temperature with equal volumes of 1 *N* sodium bicarbonate until solution was complete. The phthalic anhydride required fourteen hours and fifteen hours while the fluorenone anhydride required seventeen and eighteen and one-half hours. These values must be considered as only roughly qualitative but it seemed reasonable to believe that, allowing for such unknown factors as state of subdivision and solubility in water, a Mills–Nixon effect would have produced a greater difference.

2-Benzoylfluorenone-3-carboxylic acid was formed when 0.5 g. of the above anhydride in 15 cc. of thiophene-free benzene at 5° was treated with 0.90 g. of anhydrous aluminum chloride and the mixture then refluxed for two hours. The yield of yellow prisms from acetic acid (m. p. 247–250°) was 0.61 g. or 93%. *Anal.* Calcd. for $C_{21}H_{12}O_4$: C, 76.80; H, 3.69. Found: C, 77.03; H, 3.83.

Its **methyl ester** separated from methanol in tiny, yellow prisms, m. p. 185–187°.

Anal. Calcd. for $C_{22}H_{14}O_4$: C, 77.18; H, 4.12. Found: C, 76.84; H, 4.23.

Decarboxylation of the acid by quinoline and copper carbonate at 210° gave a compound which after crystallization from methanol and benzene-ligroin formed yellow needles, m. p. 173–174°. A mixed melting point of this material with some freshly prepared 2-benzoylfluorene[14] showed no depression, thus proving orientation.

Refluxing of a solution of aniline and fluorenone-2,3-dicarboxylic acid gave an **anil** which crystallized from aniline in fine yellow needles m. p. 310–312°. *Anal.* Calcd. for $C_{21}H_{11}O_3N$: N, 4.31. Found: N, 3.91.

Summary

Fluorenone-2,3-dicarboxylic acid, its anhydride and anil have been prepared and the anhydride has been found not to differ noticeably from phthalic anhydride in its reactions, thus indicating very little strain due to a possible Mills–Nixon effect.

It seems that with two identical substituents in positions 2 and 3 of fluorenone, that in position 2 is the more reactive.

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[14] Fortner, *Monatsh.*, **23**, 921 (1902).

HARTFORD, CONNECTICUT RECEIVED JULY 9, 1941

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

The Synthesis of Some 3-(β-Hydroxyethyl)-pyrimidines and of a 3-(β-Hydroxyethyl)-uric Acid[1]

BY ALAN HART NATHAN[1a] AND MARSTON TAYLOR BOGERT

Paralleling recent investigations[2] in these laboratories on pyrimidine and purine derivatives of cystamine, we have prepared and studied some of the analogous 3-(β-hydroxyethyl) compounds, using ethanolamine (I) as initial material and, in the main, following the familiar Traube[2b,3] procedure for the synthesis of the 3-(β-hydroxyethyl)-4,5-diaminouracil (V), fusion of which with urea yielded the desired 3-(β-hydroxyethyl)-uric acid (VI). Oxazolidino-pyrimidines and -purines should be obtainable from these ethanolamine products, but we have not as yet carried out any experiments in that direction.

It is believed that it will be of interest to examine the physiological effects of the hydroxyethyl uric acid, because its solubility in water is much greater than that of uric acid itself. Further, the Farbenfabr. vorm. F. Bayer & Co., took out a patent[4] in 1906, covering 1-(β-hydroxyethyl)-theobromine, 7-(β-hydroxyethyl)-theophylline, and 3-methyl-1,7-di-(β-hydroxyethyl)-xanthine, claiming that these derivatives exhibited the diuretic activity of the parent compounds without their undesirable side effects.

Acknowledgments.—We are indebted to the Carbide & Carbon Chemicals Corp., of New York, N. Y., for the ethanolamine used in this research, and welcome this opportunity of expressing our gratitude. Our thanks are due also to Mr. Saul Gottlieb, of these laboratories, who carried out the analytical work required.

Experimental Part

All melting points are corrected unless otherwise stated.

β-Hydroxyethylurea (II) was prepared by the action of nitrourea upon ethanolamine, as described by Charlton and Day.[5]

3-(β-Hydroxyethyl)-4-iminobarbituric Acid (III).—The absolute ethanol used in this reaction was prepared as described by Lund and Bjerrum.[6] Three grams of sodium was dissolved in 80 cc. of this absolute alcohol, and to this solution there were added 7 g. of the ethanolurea (II) and 7.6 g. of ethyl cyanoacetate. The mixture was refluxed for fourteen hours protected from moisture. Approximately

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[1] Presented in abstract before the Division of Organic Chemistry, April 10, 1940, at the Cincinnati Meeting of the American Chemical Society.

[1a] Present address: The Upjohn Co., Kalamazoo, Michigan.

[2] (a) Mills and Bogert, THIS JOURNAL, **62**, 1173 (1940); (b) Nathan and Bogert, *ibid.*, **63**, 2361 (1941).

[3] (a) Traube, *Ber.*, **33**, 1371, 3036 (1900); (b) Conrad, *Ann.*, **340**, 310 (1905).

[4] German Patent 191,106 (1906); *Chem. Zentr.*, **79**, I, 499 (1908).

[5] Charlton and Day, *J. Org. Chem.*, **1**, 552 (1936).

[6] Lund and Bjerrum, *Ber.*, **64**, 210 (1931).