

of the absorption maxima (in the near ultraviolet) calculated from the Sellmeir dispersion formula are in agreement with the wave lengths of the absorption maxima actually observed.

5. Electronic formulas for the furan ring have been proposed and discussed briefly from the standpoint of interpretation of reactions of furan derivatives.

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## SOME ARSONIC ACIDS OF FLUORENE AND ITS DERIVATIVES

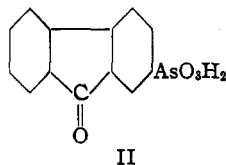
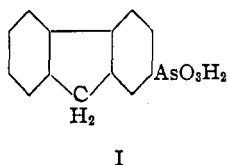
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RECEIVED NOVEMBER 21, 1930

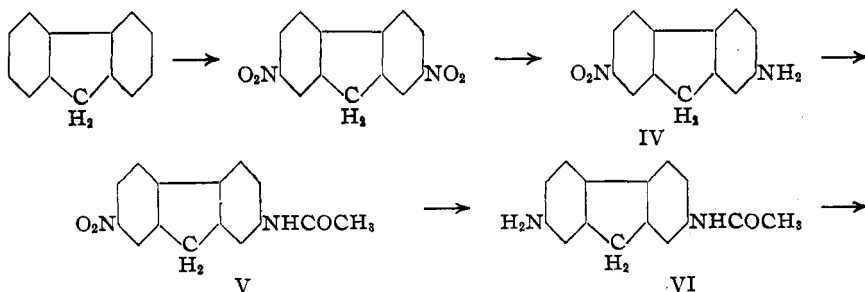
PUBLISHED FEBRUARY 9, 1931

In an attempt to find arsenicals which might be of value from the standpoint of chemotherapy, it seemed desirable to make a study of arsonic acids of fluorene and of some of its derivatives.<sup>2</sup>

Bart's<sup>3</sup> method of preparing arylarsonic acids was adapted to the preparation of 2-arsonofluorene (I), 2-arsonofluorenone (II) and 2-acetamino-



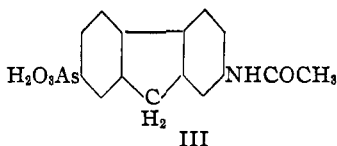
7-arsonofluorene (III). In the preparation of (III) the steps taken are indicated graphically below; the yield of (III) from (VI) was extremely low.



<sup>1</sup> This article is an abstract of Part II of a thesis submitted to the Graduate School of Northwestern University by F. E. Cislak in partial fulfillment of the requirements for the degree of Doctor of Philosophy. The work was made possible by a grant from Parke, Davis and Company.

<sup>2</sup> Some of the compounds described in this article are being tested pharmacologically at the University of Wisconsin under the direction of Dr. A. L. Tatum, but no data are available at this time.

<sup>3</sup> Bart, *Ann.*, **429**, 55 (1922).



2-Amino-7-nitrofluorene (IV) was first prepared by Diels.<sup>4</sup> By the nitration of 2-acetaminofluorene in glacial acetic acid, he obtained a mixture of 1-nitro-2-acetaminofluorene and 2-acetamino-7-nitrofluorene. This mixture could not be separated, but after hydrolysis the nitroaminofluorenes could be separated with difficulty. Because of the difficulty in obtaining any quantity of 2-acetamino-7-nitrofluorene by this procedure, a method was devised for the preparation of the desired substance in yields of 90–95% of the calculated amount.

The compounds, 2-acetamino-7-nitrofluorene, 2-acetamino-7-amino-fluorene, as well as arsonic acids of fluorene have not been reported previously in the literature.

### Experimental

**2-Nitrofluorene and 2-Aminofluorene.**—These compounds were prepared by the methods devised by Diels.<sup>5</sup>

**2-Arsonofluorene.**—Fifteen grams of 2-aminofluorene was mixed with 550 cc. of water, treated with 20 cc. of concd. hydrochloric acid solution and heated to boiling. The resulting clear solution was cooled (40°) rapidly, thereby causing the precipitation of the hydrochloride of 2-aminofluorene. While stirring this mass, a saturated aqueous solution of 6 g. of sodium nitrite was added dropwise. The hydrochloride of 2-aminofluorene then disappeared and a clear brownish yellow solution resulted. This solution was gradually heated to 60°, filtered hot and the filtrate cooled to 20°, causing the precipitation of golden yellow needles of fluorene diazonium chloride.

Thirteen grams of sodium meta-arsenite and 1 gram of copper sulfate were dissolved in 300 cc. of water. This solution was stirred during the entire course of the arsonation. In small portions, the mixture of solid fluorene diazonium chloride and its saturated solution was added to the arsenite at room temperature. At once a vigorous evolution of nitrogen occurred. Sufficient 6 N sodium hydroxide solution was added from time to time to make this arsenite solution just alkaline. When all of the diazo compound had been added, the solution was stirred for fifteen hours. The mixture was then heated to 90° and stirred for three-quarters of an hour. It was filtered hot, and the filtrate acidified with 10 cc. of concd. hydrochloric acid solution, thereby precipitating 2-arsonofluorene. This precipitate was removed by filtration, washed with water, dissolved in a dilute solution of sodium carbonate, reprecipitated with hydrochloric acid and again separated by filtration, washed and dried; yield 4.5 g.

*Anal.* Calcd. for  $C_{13}H_{11}O_3As$ : As, 25.86. Found: As, 25.71, 25.81.

**2-Nitrofluorenone and 2-Aminofluorenone.**—The preparation of these compounds has been described by Diels.<sup>6</sup>

**2-Arsonofluorenone.**—Ninety cc. of concd. hydrochloric acid solution was added to one liter of water and the solution heated to 80°. Thirty grams of 2-aminofluorenone

<sup>4</sup> Diels, *Ber.*, **35**, 3284 (1902).

<sup>5</sup> Diels, *ibid.*, **34**, 1758 (1901).

<sup>6</sup> Diels, *ibid.*, **34**, 1864 (1901).

was added to the hot solution and while stirring this mixture, it was heated to 97° until all of the solid dissolved. The resulting golden-colored solution was quickly cooled to 50°; at this temperature, the golden needles of 2-aminofluorenone hydrochloride crystallized from the solution. While stirring this mixture, a saturated aqueous solution of 14 g. of sodium nitrite was added drop by drop. After all of the nitrite solution had been added, the mixture was stirred for fifteen minutes more and then cooled to 15°.

Twenty-five grams of sodium meta-arsenite and 2 g. of copper sulfate were dissolved in 400 cc. of water. While stirring the arsenite solution, the solution of fluorenone diazonium chloride was added in small portions. A vigorous evolution of nitrogen occurred. The procedure from this point was the same as outlined under 2-arsenofluorene; yield, 10 g.

*Anal.* Calcd. for  $C_{13}H_9O_4As$ : As, 24.67. Found: As, 24.60, 24.53.

**2,7-Dinitrofluorene.**—For the preparation of this compound the directions given by Morgan and Thomson<sup>7</sup> were followed.

**2-Amino-7-nitrofluorene.**—To a solution of 1800 cc. of 95% alcohol and 200 cc. of concd. ammonia was added 30 g. of 2,7-dinitrofluorene. This solution was maintained just below its boiling point and a stream of hydrogen sulfide was passed in for four hours. At the end of the first hour the solution changed its original yellow color to a deep red and a red solid began to crystallize from the solution. At the end of the four-hour reduction period, 250 cc. of water was added to the mixture and the latter cooled to about 10°. The red precipitate formed was removed by filtration. The 2-amino-7-nitrofluorene was isolated from this precipitate by boiling the latter with 16 liters of water to which had been added 1500 cc. of concd. hydrochloric acid solution. This solution was filtered hot, the filtrate cooled and then made alkaline by the addition of an excess of ammonia solution. The precipitated orange-red 2-amino-7-nitrofluorene was filtered, washed with water and then with 100 cc. of alcohol. It was dried at 100°; yield, 90–94%. Crystallization from alcohol gave a product melting at 228–229° (corr.).

When this compound was mixed with some 2-amino-7-nitrofluorene prepared by the method of Diels,<sup>4</sup> there was no change in melting point.

**2-Acetamino-7-nitrofluorene.**—Forty-five grams of 2-amino-7-nitrofluorene was dissolved in 400 cc. of hot glacial acetic acid. To this solution were added ten 25-cc. portions of acetic anhydride, the solution being stirred after the addition of each portion. When all of the acetic anhydride had been added, the solution was refluxed for eight hours and filtered hot, thereby removing a slight amount of dark brown sediment which had formed. To precipitate the bright yellow acetylated product, the filtrate was poured into four volumes of water. It was removed by filtration, washed with 25 cc. of hot glacial acetic acid, and dissolved in 600 cc. of hot glacial acetic acid. The acetic acid solution was boiled with decolorizing carbon, filtered and the resulting filtrate diluted with 50 cc. of water and cooled to about 10°. The 2-acetamino-7-nitrofluorene crystallized from this solution. It was removed by filtration, washed several times with water and finally with two 100-cc. portions of 95% alcohol; yield, 75% of the calcd. amount. Crystallization from alcohol gave a product melting at 250–253° (corr.).

*Anal.* Calcd. for  $C_{15}H_{12}N_2O_3$ : N, 10.46. Found: N, 10.18, 10.23.

**2-Acetamino-7-aminofluorene.**—Thirty grams of 2-acetamino-7-nitrofluorene was dispersed in 700 cc. of 95% alcohol. To this were added 50 cc. of water, 100 g. of zinc dust, and a solution of 5 g. of calcium chloride in 20 cc. of water. This mixture was refluxed for five hours under mechanical stirring and filtered hot to remove the excess

<sup>7</sup> Morgan and Thomson, *J. Chem. Soc.*, 691 (1926).

zinc. This zinc was washed on the filter paper with 20 cc. of hot alcohol and then boiled with 200 cc. of 95% alcohol and separated from the alcohol by filtration. All the filtrates were combined and added to four volumes of water, thus precipitating white 2-acetamino-7-aminofluorene, which slowly acquired a gray color. This compound was removed by filtration and washed with water. In order to purify the resulting product, it was dispersed in 1 liter of hot water (90°) and to this was added 15 cc. of concd. hydrochloric acid solution, thus causing nearly all of the substance to go into solution. The mixture was filtered hot and the 2-acetamino-7-aminofluorene was reprecipitated from the filtrate by the addition of an excess of ammonia solution, filtered, washed with water and dried; yield, 60–65% of the calcd. amount. Upon recrystallization from alcohol, the compound decomposed at 188–192° (corr.).

*Anal.* Calcd. for  $C_{15}H_{14}N_2O$ : N, 11.74. Found: N, 11.56, 11.78.

**2-Acetamino-7-arsonofluorene.**—No satisfactory method has been found for preparing this substance. The method described below gave only small yields.

One liter of water was heated to 70° and to it was added 75 cc. of concd. hydrochloric acid and while stirring this solution, 15 g. of 2-acetamino-7-aminofluorene was added. The stirring at 70° was continued for fifteen minutes. Then the solution was cooled to 30° and while stirring, an aqueous solution of 6 g. of sodium nitrite was added drop by drop. After all of the nitrite solution had been added the solution was stirred for thirty minutes.

Fifteen grams of sodium meta-arsenite and a crystal of copper sulfate, the size of a pea, were dissolved in 200 cc. of water. The arsenite solution was stirred mechanically while the diazo solution was added in small portions. A copious evolution of nitrogen took place. After each portion of the diazo solution was added, the arsonation mixture was rendered just alkaline to litmus by the addition of 6 *N* sodium hydroxide solution. The solution was stirred for an hour and then the temperature was raised to 70–75°, and the stirring continued for another hour. At the end of this time the mixture was made strongly alkaline by the addition of 30 cc. of 6 *N* sodium hydroxide and filtered. The filtrate, upon acidification, gave a light brown precipitate, which was filtered off, dissolved in 300 cc. of a dilute sodium carbonate solution, filtered, acidified with concd. hydrochloric acid solution and the precipitate then formed removed by filtration and dried at 60°; yield, 2–2.5%; color; dull yellow.

*Anal.* Calcd. for  $C_{15}H_{14}NO_4As$ : As, 21.61. Found: As, 21.80, 21.49.

### Summary

1. 2-Arsonofluorene, 2-arsonofluorenone and 2-acetamino-7-arsonofluorene have been prepared for the first time.
2. A method of preparing 2-acetamino-7-nitrofluorene in considerable amounts with good yields has been developed.

EVANSTON, ILLINOIS