

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENTS OF THE UNIVERSITY OF NEBRASKA AND NORTHWESTERN UNIVERSITY]

## ISOMERIC NITRO- AND AMINONAPHTHALENEARSONIC ACIDS

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The purpose of this investigation has been the study of isomeric naphthalenearsonic acids, a field in which but little work has been done. Several investigators<sup>2</sup> have reported the preparation of 4-amino-1-naphthalenearsonic acid, by the Béchamp<sup>3</sup> reaction, and certain of its derivatives, but, in most cases, the yields reported have been small. The preparations of  $\alpha$ - and  $\beta$ -naphthylarsonic acids, along with a few derivatives, have also been recorded.<sup>4</sup>

Attempts to repeat the preparation of 4-amino-1-naphthalenearsonic acid as carried out by O. and R. Adler<sup>2</sup> were unsuccessful, although Boon and Ogilvie<sup>5</sup> have reported that they were able to prepare, by the above method, a small amount of the arsonic acid, which they described as "an amphoteric substance persistently retaining its pink color."

According to Benda and Kahn<sup>2</sup> the melting point of 4-amino-1-naphthalenearsonic acid is 175°. It does not agree with the melting-point (210°) of the product obtained in this investigation, but very nearly coincides with the melting point (177°) of one of its isomers, 1-amino-2-naphthalenearsonic acid. The previous investigators did not determine the position of the arsono group, other than drawing an analogy from the reaction for the preparation of *p*-aminophenylarsonic acid. The position of the arsono group in the compounds prepared in this investigation is known beyond question. It may be that the compound already reported as 4-amino-1-naphthalenearsonic acid is really 1-amino-2-naphthalenearsonic acid, or an impure product of the 4,1-isomer.

The difficulties encountered in the separation of the isomeric mononitronaphthylamines, used as intermediates, were considerable. In most cases the methods reported in the literature were inadequate for the purpose of obtaining these substances in sufficient amounts for this work; consequently, in several instances, new methods had to be developed.

The methods of Lellmann and Remy<sup>6</sup> and of Sircar<sup>7</sup> for the separation of the isomeric mononitro- $\alpha$ -naphthylamines left much to be desired. How-

<sup>1</sup> Parke, Davis and Company Fellow.

<sup>2</sup> Benda and Kahn, *Ber.*, 41, 1676 (1908); Farb. Meister, Lucius and Bruning, German Patent 219,210; O. and R. Adler, *Ber.*, 41, 934 (1908); Adler, German Patent 205,775.

<sup>3</sup> Béchamp, *Compt. rend.*, 56, 1172 (1863).

<sup>4</sup> Hill and Ball, *THIS JOURNAL*, 44, 2052 (1922); Michaelis and Schulte, *Ber.*, 14, 913 (1881).

<sup>5</sup> Boon and Ogilvie, *Pharm. J.*, 101, 129 (1918).

<sup>6</sup> Lellmann and Remy, *Ber.*, 19, 797 (1886).

<sup>7</sup> Sircar, *J. Chem. Soc.*, 109, 772 (1916).

ever, it was found that the separation could be readily accomplished by saturating an alcoholic solution of the mixture with dry hydrogen chloride. The 1-nitro-4-aminonaphthalene precipitated as the hydrochloride, leaving the 2-nitro-1-aminonaphthalene in solution.

The nitration of  $\beta$ -naphthylamine was first reported by Liebermann and Jacobson.<sup>8</sup> A modification of this method by Friedlaender and Littner<sup>9</sup> was a great improvement over the original method, but it was not entirely satisfactory. Small quantities of 1-nitro-2-acetylaminonaphthalene were obtained but all attempts to hydrolyze this compound led to tar formation. The use of a methyl alcohol solution of potassium hydroxide instead of an ethyl alcohol solution prevented the formation of tar. Investigations of the methods of Veselý and Jakeš<sup>10</sup> and of Hodgson and Kilner,<sup>11</sup> presented certain objectionable features so that a method was finally developed which gave good yields of 1-nitro-2-aminonaphthalene, 6-nitro-2-aminonaphthalene and 8-nitro-2-aminonaphthalene.

The corresponding arsonic acids were prepared from 2-nitro-1-aminonaphthalene, 4-nitro-1-aminonaphthalene, 1-nitro-2-aminonaphthalene and 8-nitro-2-aminonaphthalene, as well as certain derivatives. These arsonicals were analyzed for arsenic by the method of Cislak and Hamilton.<sup>12</sup>

### Experimental

**Nitration and Separation of the Isomeric Nitro-1-aminonaphthalenes.**—To 100 g. of  $\alpha$ -naphthylamine and 500 cc. of glacial acetic acid was added 83 cc. of acetic anhydride. The solution was stirred rapidly with a mechanical stirrer for fifteen minutes, and then the beaker was placed in an ice-bath and the stirring continued. As soon as the acetylated material began to form a white precipitate, 53 cc. of nitric acid (sp. gr. 1.4) was added drop-wise. When the addition of the nitric acid had been completed, the solution was stirred for one-half hour and 12 g. of sodium carbonate was then slowly added. After remaining in the refrigerator overnight, the mixture was filtered and thoroughly washed with 50% acetic acid. The product consisted of a mixture of 4-nitro-1-acetylaminonaphthalene and 2-nitro-1-acetylaminonaphthalene.<sup>6</sup>

This mixture was placed in a three-liter round-bottomed flask and dissolved in two liters of methyl alcohol. A continuous stream of dry hydrogen chloride was then allowed to bubble through the solution. At the end of three hours a light flocculent precipitate began forming and when the precipitate became heavy enough to interfere with the passage of hydrogen chloride through the solution, the precipitate was removed by filtration. The filtrate, consisting mainly of 2-nitro-1-aminonaphthalene, was returned to the flask and the process continued. The compound which precipitated was the hydrochloride of 4-nitro-1-aminonaphthalene. This product (53 g.) was converted to the free base by neutralizing with dilute alkali and recrystallizing from hot alcohol; yield, 40 g.; m. p. 191°.<sup>13</sup>

<sup>8</sup> Liebermann and Jacobson, *Ann.*, 211, 36 (1882).

<sup>9</sup> Friedlaender and Littner, *Ber.*, 48, 329 (1915).

<sup>10</sup> Veselý and Jakeš, *Bull. soc. chim.*, [4] 33, 942 (1923).

<sup>11</sup> Hodgson and Kilner, *J. Chem. Soc.*, 192, 8 (1926).

<sup>12</sup> Cislak and Hamilton, *THIS JOURNAL*, 52, 638 (1930).

<sup>13</sup> Liebermann, *Ann.*, 183, 232 (1876); Kleemann, *Ber.*, 19, 338 (1886).

The filtrate, from which the 4-nitro-1-aminonaphthalene was removed as the hydrochloride, was concentrated on a water-bath to about 500 cc., decolorized with activated charcoal and filtered. The crystals which separated on standing were recrystallized twice from hot alcohol and identified as 2-nitro-1-aminonaphthalene; yield, 20 g.; m. p. 143°. <sup>14</sup>

**Nitration and Separation of the Isomeric Mononitro-2-aminonaphthalenes.**—To a solution of 200 g. of  $\beta$ -naphthylamine in 200 cc. of glacial acetic acid was added 150 cc. of acetic anhydride and the mixture stirred for fifteen minutes with a mechanical stirrer, after which the beaker containing the solution was cooled in an ice-bath and the stirring continued. In about ten minutes the acetylated material began to crystallize and at this point a further 100 cc. of glacial acetic acid was added. The temperature of the bath was then lowered by the addition of salt, and 110 cc. of concentrated nitric acid was added drop-wise over a period of three hours. After standing for several hours, the product was filtered, sucked dry and washed thoroughly with ether. <sup>15</sup> The product consisted of a mixture of 1-nitro-2-acetylaminonaphthalene, 8-nitro-2-acetylaminonaphthalene and an appreciable quantity of 6-nitro-2-acetylaminonaphthalene; yield of isomers, 260 g.

Hydrolysis of the mixture of isomers was effected by refluxing a solution of the product (125 g.) in alcohol (500 cc.) with concentrated hydrochloric acid (125 cc.) for four hours. The solution was then poured into three liters of cold water and the crude 1-nitro-2-aminonaphthalene filtered off, dried and recrystallized from twice its weight of hot alcohol; yield, 75 g., m. p. 127°. <sup>16</sup>

The filtrate, containing the soluble hydrochloride of 8-nitro-2-aminonaphthalene and 6-nitro-2-aminonaphthalene, was made alkaline to litmus with 6 *N* sodium hydroxide and immediately an orange-red precipitate formed. This was filtered off, washed with water and allowed to air dry. The product was then added to one liter of alcohol and heated to boiling on a hot-plate. A considerable portion of the material did not dissolve. After standing for a number of hours the gold colored crystals of 6-nitro-2-aminonaphthalene were filtered off, washed with cold alcohol and dried; yield, 8 g.; m. p. 203°. <sup>10</sup>

The filtrate from which the 6-nitro-2-aminonaphthalene had been removed was concentrated to 100 cc. and cooled in order to precipitate the dark red crystals of 8-nitro-2-aminonaphthalene. These were removed by filtration, washed with water and dried in the air; yield, 24 g.; m. p. 103.5°. <sup>17</sup>

#### Arsonation of the Isomeric Nitro-aminonaphthalenes

**4-Nitro-1-naphthalenearsonic Acid.**—One-tenth of a mole (18.8 g.) of 1-nitro-4-aminonaphthalene was placed in a 600-cc. beaker and 200 cc. of 6 *N* hydrochloric acid added. The beaker containing the mixture was then placed in an ice-bath and equipped with a mechanical stirrer. After the contents of the beaker had dropped below 5°, a solution of sodium nitrite (8 g. of sodium nitrite in 50 cc. of water) was slowly added with constant stirring during a period of one hour. The diazonium solution was then added directly to three liters of an ice cold solution of sodium metaarsenite. The arsenite solution was prepared by dissolving 39 g. of sodium metaarsenite and a few crystals of copper sulfate in a liter of water and making up the total volume to three liters by the addition of crushed ice. The mixture was stirred rapidly by means of a me-

<sup>14</sup> Lellmann and Remy, *Ber.*, 19, 802 (1886); Liebermann, *Ann.*, 183, 246 (1876).

<sup>15</sup> Caution should be taken to prevent water from coming in contact with the product before washing with ether, otherwise, a tar is produced.

<sup>16</sup> Liebermann and Jacobson, *Ann.*, 211, 64 (1882).

<sup>17</sup> Friedländer and St. Szymanski, *Ber.*, 25, 2077 (1892).

chanical stirrer and then 220 cc. of 5*N* sodium hydroxide solution was added dropwise. The solution at this point reacted slightly alkaline to litmus paper. Stirring was continued for one-half hour longer to ensure complete coupling and then the solution was filtered. The filtrate was made acid to Congo red paper with hydrochloric acid and immediately a flocculent, light yellow precipitate of 4-nitro-1-naphthalenearsonic acid appeared. The precipitate was filtered off, reprecipitated once from *N*/2 sodium carbonate solution by means of hydrochloric acid and dried in an oven at 100°, yield, 23.7 g. (80%). The compound did not melt or decompose below 250°.

*Anal.* Calcd. for  $C_{10}H_8NAsO_5$ : As, 25.25. Found: As, 25.07, 25.00.

**4-Amino-1-naphthalenearsonic Acid.**—The method employed for the preparation of this compound was a slight modification of that described by Johnson and Adams.<sup>18</sup> It consisted essentially of the reduction of a nitro-arylarsonic acid to the corresponding aminoarylarsonic acid by means of freshly prepared ferrous hydroxide.

**2-Nitro-1-naphthalenearsonic Acid.**—Ten grams of 2-nitro-1-aminonaphthalene was dissolved in 100 cc. of hot glacial acetic acid. To this solution was added a mixture of 30 cc. of concentrated sulfuric acid and 50 cc. of water. The amine quickly separated as a fine paste. The beaker was then placed in an ice-bath and stirred with a mechanical stirrer. When the temperature of the mixture in the beaker had dropped below 5°, a solution of sodium nitrite (6.9 g. of sodium nitrite in 50 cc. of water) was added drop by drop over a period of two hours. When diazotization was complete the diazonium solution was added directly to two liters of an ice-cold solution of sodium metaarsenite (containing 30 g. of sodium metaarsenate) and a few crystals of copper sulfate. The acidity of the solution was neutralized by slowly adding 6 *N* sodium hydroxide and the solution finally made slightly alkaline by the addition of a few cc. of alkali in excess. The solution was allowed to stand overnight, filtered and the filtrate made acid to Congo red paper. A bright yellow precipitate of 2-nitro-1-naphthalenearsonic acid appeared immediately; yield, 10.2 g. (65%). The compound was reprecipitated once from dilute sodium carbonate solution with hydrochloric acid and analyzed. It proved to be practically insoluble in hot water but dissolved readily in hot alcohol from which it crystallized in well-defined yellow needles. It melted with decomposition at 202°.

*Anal.* Calcd. for  $C_{10}H_8NAsO_5$ : As, 25.25. Found: As, 25.11, 25.23.

**2-Amino-1-naphthalenearsonic Acid.**—The method used for the reduction of 2-nitro-1-naphthalenearsonic acid to 2-amino-1-naphthalenearsonic acid was the same as that employed for the reduction of 1-arsono-4-nitronaphthalene; a yield of 88% of the calculated amount was obtained. The compound shrivelled and darkened in the m. p. tube at 174°, and finally decomposed around 216°.

*Anal.* Calcd. for  $C_{10}H_{10}NAsO_5$ : As, 28.09. Found: As, 28.25, 28.20.

**1-Nitro-2-naphthalenearsonic Acid.**—One-tenth of a mole (18.8 g.) of 1-nitro-2-aminonaphthalene was diazotized and coupled with sodium metaarsenite following the procedure developed for the preparation of 2-nitro-1-naphthalenearsonic acid. The compound was practically insoluble in cold alcohol but dissolved readily in hot alcohol, from which it crystallized in thin yellow plates. It melted with decomposition at 192°; yield, 20.2 g. (68%).

*Anal.* Calcd. for  $C_{10}H_8NAsO_5$ : As, 25.25. Found: As, 25.24, 25.24.

The monosodium salt of 1-nitro-2-naphthalenearsonic acid was yellow in color and very insoluble. A solution containing 35 g. of the arsono acid in 500 cc. of *N*/2 sodium carbonate was made neutral to litmus paper with hydrochloric acid and on standing for

<sup>18</sup> Johnson and Adams, *THIS JOURNAL*, 45, 1312 (1923).

a short time flaky yellow crystals of the monosodium salt began to deposit on the bottom of the beaker.

**1-Amino-2-naphthalenearsonic Acid.**—This compound was prepared by reducing with ferrous hydroxide, following the directions used in the preceding reductions. One tenth of a mole gave 23.4 g. of 1-amino-2-naphthalenearsonic acid (88% yield) on reduction. It melted with decomposition at 177°.

The compound was practically insoluble in cold but very soluble in hot alcohol, acetone, glacial acetic acid and benzene. It was only slightly soluble in hot water and ether.

*Anal.* Calcd. for  $C_{10}H_{10}NAsO_3$ : As, 28.09. Found: As, 27.96, 27.91.

**8-Nitro-2-naphthalenearsonic Acid.**—Fifteen and four-tenths grams of 8-nitro-2-aminonaphthalene was diazotized and coupled with sodium metaarsenite in the usual manner. The solution containing the arsonic acid was filtered and acidified with hydrochloric acid. The creamy white precipitate which formed was removed by filtration and dissolved in *N*/2 sodium carbonate solution, filtered and reprecipitated by hydrochloric acid in a very pure condition; yield, 10.6 g. (43.6%). The compound did not melt or decompose under 265°.

*Anal.* Calcd. for  $C_{10}H_8NAsO_5$ : As, 25.25. Found: As, 25.10, 25.14.

**8-Amino-2-naphthalenearsonic Acid.**—A 5-g. sample of 8-nitro-2-naphthalenearsonic acid was reduced by means of freshly prepared ferrous hydroxide. A clear filtrate was obtained on filtering the reaction mixture which when acidified with hydrochloric acid gave a white precipitate of 8-amino-2-naphthalenearsonic acid that rapidly changed to a pink and finally to a brown color on standing a short time in contact with the air. The compound was not recovered in a pure condition. The yield of crude product was 68%.

*Anal.* Calcd. for  $C_{10}H_{10}NAsO_3$ : As, 28.09. Found: As, 27.58, 27.51.

**4-Benzeneazo-1-naphthalenearsonic Acid.**—To a hot solution of 10 cc. of concentrated sulfuric acid and 50 cc. of water in a 400-cc. beaker was slowly added 12 cc. of aniline with constant stirring. After the aniline had gone into solution, 150 cc. of water was added and the beaker placed in an ice-bath. When the temperature had dropped below 5°, a solution of sodium nitrite (10 g. in 50 cc. of water) was slowly added with constant stirring until a drop of the reacting mixture gave a permanent blue color to starch-iodide paper.

The diazonium solution was slowly added to a warm alcoholic solution of  $\alpha$ -naphthylamine (15.6 g.  $\alpha$ -naphthylamine in 600 cc. of alcohol) in a liter beaker. The mixture was stirred for one-half hour and then poured into two liters of water. Immediately a brown amorphous product precipitated. The reaction proceeded almost quantitatively.

One-tenth of a mole (35.6 g.) of the dye thus formed was dissolved in 100 cc. of glacial acetic acid in a 600-cc. beaker and cooled rapidly with constant stirring. To this solution was added 30 cc. of concentrated sulfuric acid and 60 cc. of water. The beaker was then placed in an ice-bath and a solution of sodium nitrite (10 g. in 50 cc. of water) was added drop-wise over a period of two hours. At the end of this time diazotization was assumed to be complete and the diazonium solution was added directly to two liters of an ice-cold solution of 39 g. of sodium metaarsenite containing a few crystals of copper sulfate. The solution was gradually neutralized by the addition of 6*N* sodium hydroxide and then a few cc. in excess was added. The resulting mixture was filtered and the filtrate made acid to Congo red paper with hydrochloric acid. A red precipitate formed immediately which recrystallized from hot alcohol in the form of reddish-yellow plates. The yield, however, was very small (8%).

*Anal.* Calcd. for  $C_{16}H_{13}N_2AsO_3$ : As, 21.07. Found: As, 20.90, 21.02.

TABLE I  
DERIVATIVES OF AMINONAPHTHALENEARSONIC ACIDS

Name, -naphthalenearsonic acid	Yield, %	M. p., °C.	Arsenic analyses, %	
			Calcd.	Found
4-Acetylamino-1	90	271 dec.	24.27	24.15
4-Carboethoxyamino-1	90	250	22.12	22.03
4-β-Hydroxyethyl-1	65	250	24.11	24.03
1-Acetylamino-2	72	240-245 dec.	24.27	24.24
1-Carboethoxyamino-2	95	191 dec.	22.12	21.93

### Summary

Better methods have been developed for the separation of the isomeric nitroaminonaphthalenes formed by the nitration of  $\alpha$ - and  $\beta$ -naphthylamines, thus permitting their preparation on a large scale.

The nitroaminonaphthalenes have been arsonated and the products, 4-nitro-1-naphthalenearsonic acid, 2-nitro-1-naphthalenearsonic acid, 1-nitro-2-naphthalenearsonic acid, and 8-nitro-2-naphthalenearsonic acid have been isolated, the last three for the first time.

The isomeric nitronaphthalenearsonic acids have been reduced to the corresponding aminonaphthalenearsonic acids and several derivatives of these have been prepared.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

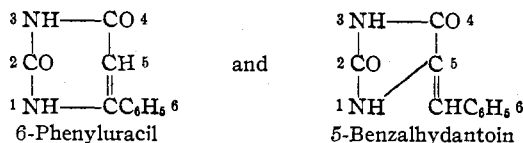
## ULTRAVIOLET ABSORPTION SPECTRA OF SOLUTIONS OF SOME SUBSTITUTED PHENYLURACILS<sup>1</sup>

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Uracil and hydantoin are quite similar in many ways. Both are urea derivatives, both form sodium salts and both can be alkylated. A comparison of the alkylation products obtained from 6-phenyluracil<sup>2</sup> and the isomeric 5-benzalhydantoin<sup>3</sup> shows analogous changes in physical properties such as melting point and solubility.



In the benzal- and anisalhydantoin series, considerable differences in the

<sup>1</sup> Constructed from a dissertation presented by Janet Evans to the Faculty of the Graduate School of Yale University, in June, 1929, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

<sup>2</sup> Evans and Johnson, *THIS JOURNAL*, **52**, 4993 (1930).

<sup>3</sup> Hahn and Evans, *ibid.*, **50**, 806 (1928).