age. A quantity has been prepared and will be kept until a year hence when it is hoped that this study can be resumed.

UNIVERSITY OF SOUTH DAKOTA,
VERMILLION, S. DAK.
December 18, 1905.

---

[CONTRIBUTIONS FROM THE HAVEMEYER LABORATORIES OF COLUMBIA UNIVERSITY. NO. 121.]

# ON DIMETHYL 4-AMINOPHTHALATE AND CERTAIN OF ITS ACYL DERIVATIVES.

BY MARSTON TAYLOR BOGERT AND ROEMER REX RENSHAW.

Received January 11, 1906.

AS A sequel to the work on the nitro-*o*-phthalic acids recently conducted in this laboratory,[1] we have turned our attention to the aminophthalic acids also.

Very little information appears in the literature concerning 4-aminophthalic acid or its derivatives. It seemed of interest, therefore, to prepare a number of its derivatives and study their properties.

As the free 4-aminophthalic acid is not readily obtained pure, on account of its instability, we used its dimethyl ester as the starting point for our experiments. This was prepared from phthalic anhydride by nitrating, esterifying the mixture of nitro acids which result; separating the neutral ester of the 4-nitrophthalic acid, and then reducing the nitro acid with alcoholic hydrochloric acid and zinc dust. By this method, the amino ester was obtained in satisfactory yield and purity. Quite lately, Cohen and McCandlish[2] tried to reduce the nitrophthalic ester with hydrogen sulphide, but could get no pure product, the amino ester formed being invariably contaminated with a yellow, viscid oil, which they thought was probably a sulphur compound.

From the dimethyl ester, we prepared the following derivatives: hydrochloride; a dimolecular condensation product with formic acid; acetyl, propionyl, isobutyryl, benzoyl, *m*- and *p*-nitrobenzoyl, urethane, phenyluramino, ethoxalyl, oxalyl, phthalamic acid, succinamic acid, and the silver salts of both the latter; also 4-aminophthalanil.

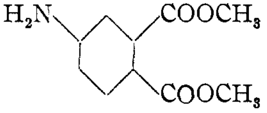
---

[1] Bogert and Boroschek: This Journal, 23, 740 (1901); Bogert and Wright: Ibid. 27, 1310 (1905.)

[2] J. Chem. Soc. 88, 1269 (1905).

## EXPERIMENTAL PART.

*Preparation of Dimethyl 4-Aminophthalate,*



—Phthalic anhydride was nitrated as described by Bogert and Boroschek,[1] and the resulting mixture of 3- and 4-nitrophthalic acids partially separated by fractional crystallization. Two hundred grams of the crude 4-nitro acid thus separated were boiled for eight hours with 320 grams of methyl alcohol and 60 grams of concentrated sulphuric acid. The 4-nitro acid is thus changed to the neutral dimethyl ester, while any 3-nitro acid present forms mainly the acid monomethyl ester. The excess of methyl alcohol was evaporated, the residue poured into cold water, the oily ester layer separated and agitated with an excess of sodium carbonate solution. The acid ester is dissolved by this treatment, while the neutral ester remains undissolved as a waxy solid. The crude neutral ester was thoroughly washed with water, and purified by recrystallization from alcohol.

The dimethyl 4-nitrophthalate was reduced by alcoholic hydrochloric acid and zinc dust, as described by Baeyer,[2] Miller,[3] Edinger,[4] Onnertz[5] and others, for the corresponding diethyl ester. Fifty grams of the nitro ester were treated with 250 grams of alcohol and 500 grams of concentrated hydrochloric acid. The mixture was cooled to 0°, stirred with a turbine, and small amounts of zinc dust added from time to time. It is advisable to continue the addition of the zinc dust for some time after all the nitro ester has dissolved, as otherwise the amino ester may be contaminated by intermediate reduction products at the close of the reduction, the solution was diluted with an equal volume of water, filtered from excess of zinc dust, and the greater part of the acid carefully neutralized with sodium hydroxide solution, the temperature being kept down by occasional additions of cracked ice. Final neutralization was accomplished by adding sodium carbonate solution as long as the precipitate which first

---

[1] Loc. cit.

[2] Ber. 10, 124, 1079 (1877).

[3] Ibid. 11, 1191 (1878).

[4] J. pr. Chem. [2] 53, 375 (1896).

[5] Ber. 34, 3735 (1901).

formed redissolved on stirring. The amino ester was then precipitated by the addition of a saturated solution of sodium acetate, and the mixture left for a few hours in the refrigerator. The amino ester separated in slightly colored glistening plates, which were filtered out, and purified by crystallization from alcohol or benzene. The yield was about 88 per cent. of the theory.

Dimethyl 4-aminophthalate crystallizes from alcohol or benzene in shining white plates; from water, in long hexagonal prisms. It melts at 84° (corr.). It is soluble in cold alcohol, acetone, chloroform, nitrobenzene, aniline, pyridine, or mineral acids; slightly soluble in hot water, carbon tetrachloride or ether; difficultly soluble in carbon disulphide or in petroleum ether.

Calculated for $C_{10}H_{11}O_4N$: C, 57.40; H, 5.30; N, 6.70. Found: C, 57.22; H, 5.26; N, 6.65.

*Hydrochloride.*—The amino ester was dissolved in dry benzene and treated with benzene saturated with dry hydrogen chloride. A gummy precipitate separated, which soon hardened to a crystalline mass. This was removed, washed with dry benzene, and dried in a vacuum desiccator. It dissolves freely in water, but soon dissociates with precipitation of the free amino ester. In a moist atmosphere, it slowly gives off hydrogen chloride.

### ACYL DERIVATIVES OF DIMETHYL 4-AMINOPHTHALATE.

### *I. Derivatives of the Acetic Acid Series.*

*Dimethyl 4-Aminophthalate and Glacial Formic Acid.*—Five grams of the amino ester were boiled for three hours with an excess of glacial formic acid. The excess of acid was then evaporated, and the residual oily material crystallized from alcoholic formic acid. In this way, a small amount of crystalline product was obtained. The mother-liquors appeared to contain one or two other substances, which, however, were not further investigated.

The substance separated by crystallization from alcoholic formic acid, forms nearly colorless microscopic crystals, m. p. 179° (corr.), which are soluble in alcohol, hot ethyl acetate, acetone, or benzene; very difficultly soluble in ether, carbon disulphide, chloroform or petroleum ether. They are apparently quite easily hydrolyzed.

On analysis, the amount of nitrogen found was 6.66 per cent. This agrees closely with the theoretical amount of nitrogen present in the dimolecular condensation product, $(CH_3OOC)_2$

$C_6H_3NHCH:NC_6H_3(COOCH_3)_2$, resulting from a condensation of the formyl derivative first produced with a second molecule of the amino ester.

Nitrogen calculated for $(CH_3OOC)_2C_6H_3NHCOH$, 5.92; nitrogen calculated for $(CH_3OOC)_2C_6H_3NHCH:NC_6H_3(COOCH_3)_2$, 6.54; nitrogen found, 6.66.

*Dimethyl 4-Acetaminophthalate*, $C_6H_3(COOCH_3)_2NHCOCH_3$.—Five grams of the amino ester were boiled for some time with an excess of acetic anhydride. The solution was then precipitated by dilution with water, the precipitate filtered out, washed thoroughly with water, and crystallized from 30 per cent. alcohol. It was thus obtained in small, colorless crystalline plates, melting at 136.5° (corr.). It dissolves in alcohol, chloroform, benzene, acetone, hot carbon disulphide, ether, or water, but is very difficultly soluble in petroleum ether.

Calculated for $C_{12}H_{13}O_5N$: N, 5.58. Found: N, 5.76.

*Dimethyl 4-Propionaminophthalate*, $C_6H_3(COOCH_3)_2NHCOC_2H_5$.—The amino ester was boiled with propionic anhydride, the propionic acid and excess of anhydride distilled off, the residual oil dissolved in alcohol, treated with bone-black, and precipitated by diluting with water and cooling in a freezing-mixture. The substance was thus obtained in crystalline condition. It was recrystallized by dissolving it in benzene and carefully adding petroleum ether.

This propionyl derivative crystallizes in long, thin, colorless needles, melting at 110.5° (corr.); soluble in alcohol, benzene, acetone, ethyl acetate, ether, or chloroform; insoluble in petroleum ether, or cold water.

Calculated for $C_{13}H_{15}O_5N$: N, 5.30. Found: N, 5.5 and 5.59.

*Dimethyl 4-Isobutyraminophthalate*, $C_6H_3(COOCH_3)_2NHCOCH(CH_3)_2$.—The amino ester was dissolved in just sufficient isobutyric anhydride to effect solution, and the solution was then boiled for an hour. On cooling, a brownish solid resulted. This was pulverized, washed with water, dissolved in alcohol, the solution treated with bone-black and cooled. The crystals which separated were purified by solution in benzene and reprecipitation with petroleum ether, or by recrystallization from dilute alcohol.

The isobutyryl derivative crystallizes in long, thin, colorless needles, melting at 122–123° (corr.), which dissolve in alcohol, benzene, chloroform, carbon disulphide, ether, or acetone, but are very difficultly soluble in water or petroleum ether.

Calculated for $C_{14}H_{17}O_5N$: N, 5.0. Found: N, 5.16.

### *II. Derivatives of the Benzoic Acid Series.*

*Dimethyl 4-Benzoylaminophthalate*, $C_6H_3(COOCH_3)_2NHCOC_6H_5$.—The amino ester was dissolved in pyridine, the calculated amount of benzoyl chloride added, and the product precipitated by the addition of water. By crystallization from benzene, it was obtained in colorless needles, melting at 132–132.5° (corr.); soluble in alcohol, benzene, acetone, chloroform, or ethyl acetate; slightly soluble in carbon disulphide; very difficultly soluble in ether, naphtha, or water.

Calculated for $C_{17}H_{15}O_5N$: N, 4.40. Found: N, 4.64.

*Dimethyl 4-m-Nitrobenzoylaminophthalate*, $C_6H_3(COOCH_3)_2NHCOC_6H_4NO_2(m)$.—The amino ester was dissolved in pyridine, treated with the calculated amount of *m*-nitrobenzoyl chloride, and the mixture heated for some time. The mixture when poured into water separated an oil. This oil was washed free from pyridine hydrochloride, dissolved in alcohol, the solution concentrated to crystals, and the crystals recrystallized from benzene.

The substance forms nearly colorless scales, melting at 147° (corr.).

Calculated for $C_{17}H_{14}O_7N_2$: N, 7.83. Found: N, 7.87.

*Dimethyl 4-p-Nitrobenzoylaminophthalate*, $C_6H_3(COOCH_3)_2NHCOC_6H_4NO_2(p)$.—This was prepared in the same way as the meta derivative just mentioned. It crystallizes from alcohol in small yellowish flakes, melting at 202° (corr.). It is slightly soluble in cold alcohol, hot amyl acetate, or hot benzene; very difficultly soluble in carbon disulphide, chloroform, or naphtha.

Calculated for $C_{17}H_{14}O_7N_2$: N, 7.83. Found: N, 7.95.

### *III. Derivatives of Carbonic Acid.*

*Dimethyl 4-Urethanophthalate*, $C_6H_3(COOCH_3)_2NHCOOC_2H_5$.—Three grams of ethyl chlorcarbonate were added to a dilute alcoholic solution containing 4 grams of the amino ester and 2 grams of sodium carbonate. The reaction was accompanied by rise of temperature and evolution of carbon dioxide, and was completed by warming for a few minutes on the steam-bath. On careful dilution with water a precipitate was obtained, which, recrystallized from boiling water, separated in long needles, melting at 122° (corr.).

This urethane is soluble in alcohol, acetone, ethyl acetate, ether, carbon tetrachloride, chloroform, or hot water; difficultly soluble in cold water, and apparently insoluble in petroleum ether.

Calculated for $C_{13}H_{15}O_6N$: N, 5.0. Found: N, 5.13.

*Dimethyl 4-Phenyluraminophthalate*, $C_6H_3(COOCH_3)_2NHCONHC_6H_5$.—Five grams of the amino ester, dissolved in dry benzene, were treated with excess of phenyl isocyanate, and the solution gently boiled for two hours. The benzene solution was then concentrated, petroleum ether carefully added, and the solution placed in an ice pack. The crystals thus obtained were purified by recrystallization from benzene.

The pure substance forms microscopic needles, melting at 138° (corr.), which are soluble in alcohol, benzene, ether, acetone, ethyl acetate, or chloroform, but very difficultly soluble in carbon disulphide, or petroleum ether.

Calculated for $C_{17}H_{16}O_5N_2$: N, 8.50. Found: N, 8.64.

### *IV. Derivatives of Bibasic Acids.*

*Dimethyl Ethoxalyl-4-aminophthalate*, $C_6H_3(COOCH_3)_2NHCOCOOC_2H_5$.—Five grams of the amino ester were heated for several hours with a slight excess of ethyl oxalate. After distilling off the alcohol formed in the reaction, there remained an oil containing a small amount of a white precipitate. On extracting with boiling alcohol, the oil was all dissolved, while the precipitate remained insoluble. On concentrating the alcoholic extracts, the ethoxalyl derivative was precipitated, and it was then purified by recrystallization from alcohol.

As thus prepared, it formed small white flakes, melting at 121.5° (corr.); soluble in alcohol, benzene, acetone, ethyl acetate, ether, chloroform, or carbon tetrachloride; very difficultly soluble in naphtha.

Calculated for $C_{14}H_{15}O_7N$: N, 4.52. Found: N, 4.77 and 4.75.

*Dimethyl Oxalyl-4-aminophthalate*, $C_6H_3(COOCH_3)_2NHCOCONHC_6H_3(COOCH_3)_2$.—The white insoluble precipitate observed in the foregoing reaction proved to be the corresponding oxalyl derivative resulting from the condensation of the ethoxalyl body with a second molecule of the amino ester. It was purified by digesting successively with alcohol, benzene, ether, and chloroform.

It is insoluble or very difficultly soluble in alcohol, benzene, ether, chloroform, acetone, ethyl acetate, carbon disulphide, nitrobenzene, petroleum ether, or water, and melts at 239° (corr.).

Calculated for $C_{22}H_{20}O_{10}N_2$: N, 5.9. Found: N, 5.68.

*Phthalamic Acid of Dimethyl 4-Aminophthalate*, $C_6H_3(COOCH_3)_2NHCOC_6H_4COOH$.—A benzene solution of 5 grams of the amino ester was added to a saturated benzene solution of phthalic anhydride, and the whole boiled until it became decidedly turbid. On concentrating and cooling, microscopic crystals separated in large amount. These crystals were purified by dissolving in amyl acetate and adding petroleum ether, or, better, by dissolving in alcohol and adding benzene. Attempts to crystallize from dilute alcohol resulted in more or less hydrolysis of the compound.

It is soluble in alcohol, acetone, or amyl acetate; slightly soluble in boiling benzene, or in ether; very difficultly soluble in water, chloroform, or petroleum ether. It melts at about 166–167° (corr.) with loss of water, probably passing thereby into the corresponding imide.

Calculated for $C_{18}H_{15}O_7N$: N, 3.93. Found: N, 3.92.

Its *silver salt* was also prepared, by precipitating the solution of the ammonium salt with silver nitrate. Washed with water and dried, it resembles silver chloride in general appearance.

Calculated for $C_{18}H_{14}O_7NAg$: Ag, 23.22. Found: Ag, 23.10.

*Succinamic Acid of Dimethyl 4-Aminophthalate*, $C_6H_3(COOCH_3)_2NHCOCH_2CH_2COOH$.—This was prepared from the amino ester and succinic anhydride in much the same way as the phthalamic compound. The succinamic derivative separated on concentrating the benzene solution and was purified by crystallization from water.

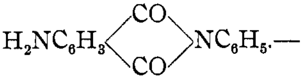
It crystallizes from water in colorless needles, melting at 173° (corr.), with loss of water and presumably with formation of the imide. It is soluble in boiling water, in alcohol, acetone, or ethyl acetate, slightly soluble in hot benzene, and very difficultly soluble in ether, chloroform, carbon tetrachloride, or naphtha.

Calculated for $C_{14}H_{15}O_7N$: N, 4.5. Found: N, 4.68 and 4.74.

By precipitating a solution of the ammonium salt with silver nitrate, the *silver salt* generally separated in a gelatinous form, but, on standing in the solution, it gradually changed to a more granular condition.

Calculated for $C_{14}H_{14}O_7NAg$: Ag, 25.94. Found: Ag, 26.06.

*4-Aminophthalanil,*



$$H_2NC_6H_3\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle NC_6H_5.—$$

Five grams of dimethyl 4-aminophthalate were dissolved in boiling aniline, and the boiling continued for a short time. An excess of acetic acid was added to the cooled solution and then water. By this dilution the anil was thrown out as a yellow precipitate, which was purified by crystallization from alcohol or from glacial acetic acid.

The pure anil crystallizes in long yellowish needles, melting at 205.5° (corr.). It is soluble in alcohol, ethyl acetate, chloroform, or benzene, when hot; slightly soluble in hot water, or cold acetic acid; very difficultly soluble in acetone, ether, carbon disulphide, or naphtha.

Calculated for $C_{14}H_{10}O_2N_2$: N, 11.80. Found: N, 11.93.

ORGANIC LABORATORY, COLUMBIA UNIVERSITY,
March, 1906.

---

# THE OPTICAL ROTATION AND THE DENSITY OF ALCOHOLIC SOLUTIONS OF GLIADIN.

BY W. E. MATHEWSON.

Received February 12, 1906.

THE recent application of the polariscope to the estimation of gliadin[1] has rendered desirable some further knowledge regarding the specific rotation of this substance. With many substances optically active in solution, the specific rotatory power changes in a marked manner with changes in temperature, concentration, and nature of the solvent. The experiments given below were carried out by the writer with the view of determining the error that might be introduced into an analytical estimation by such variations.

The gliadin used had been prepared from a hard wheat patent flour by a method used by Osborne and Voorhees.[2] A small sample dried for twenty days in a vacuum over sulphuric acid

---

[1] H. Snyder: This Journal, 24, 263.

[2] Am. Ch. J. 15, 416, preparation No. 17.