

The following figures are taken from our laboratory note-book, on metabolism. They are expressed in terms of *N*/10 ammonia.

cc. solution taken.	Specimen A.			Specimen B.			Specimen C.	
Free NH <sub>3</sub> . . . . . 25	0.65	0.70	...	0.60	0.60	...	9.00	9.05
Gross urea . . . . . 10	19.60	19.65	19.60	43.30	43.20	43.20	33.80	33.75
Total nitrogen... 10	20.50	20.50	20.60	44.30	44.30	44.10	35.60	35.70

My thanks are due to Dr. P. A. Levene and to Dr. G. W. Heimrod for their advice and encouragement in developing this method and to Mr. Wm. W. Crawford for assistance in preparing this paper for publication.

ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH,  
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[CONTRIBUTIONS FROM THE HAVEMEYER LABORATORIES OF COLUMBIA UNIVERSITY.  
No. 154.]

#### 4-AMINO-*o*-PHTHALIC ACID AND SOME OF ITS DERIVATIVES.<sup>1</sup>

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In a previous paper,<sup>2</sup> the authors described dimethyl 4-aminophthalate and certain of its acyl derivatives. The present article deals with the free acid, its salts, and various other derivatives or experiments not reported in the earlier paper.

The literature on the subject of the free 4-amino-*o*-phthalic acid is meagre and confusing.

Miller<sup>3</sup> subjected 4-nitrophthalic acid to the action of tin and hydrochloric acid. The reduction proceeded smoothly, no carbon dioxide was evolved, and presumably the double salt of tin chloride and aminophthalate was formed. This double tin salt remained in solution and could not be separated by freezing (differing in this respect from the corresponding 3-aminophthalic compound). When the tin was precipitated from this solution by hydrogen sulphide and the filtrate from the tin sulphide concentrated, only the hydrochloride of *m*-aminobenzoic acid remained.

Bodé<sup>4</sup> reduced 4-nitrophthalic acid to the double zinc acetate and aminophthalate by the Bernthsen and Semper method<sup>5</sup> but found the yield inferior to that obtained from the 3-nitro acid. These double zinc acetates and aminophthalates can be diazotized direct and thus used for the preparation of other substituted phthalic acids or for direct coupling. Apparently, he did not attempt the isolation of the free aminophthalic acid.

<sup>1</sup> Read at the New York meeting of the Society, Dec. 28, 1906.

<sup>2</sup> THIS JOURNAL, 28, 617 (1906).

<sup>3</sup> *Ber.*, 11, 992 (1878); *Ann.*, 208, 223 (1881).

<sup>4</sup> Inaug. Dissertat., Heidelberg (1898).

<sup>5</sup> *Ber.*, 19, 164 (1886).

Seidel<sup>1</sup> reduced 4-nitrophthalic acid to the amino acid by the action of sodium sulphide, but gives no details as to his method. He states that the acid crystallizes from alcohol in needles melting above 280°, but says nothing as to its relative stability.

Wegscheider and Bondi<sup>2</sup> obtained the 1-methyl ester of 4-aminophthalic acid by reducing the corresponding nitro compound, and describe it as a yellow indefinitely crystalline compound, decomposing in the vicinity of 145°, and quite stable to water or hydrochloric acid.

The neutral esters of 4-aminophthalic acid are easily prepared from the corresponding nitro esters<sup>3</sup> and are quite stable.

We have repeated Miller's work and confirmed his observations. The reduction of 4-nitrophthalic acid with tin and hydrochloric acid proceeds smoothly, without evolution of carbon dioxide, but when the tin is precipitated as sulphide and the acid filtrate concentrated, carbon dioxide gradually escapes and only *m*-aminobenzoic acid remains. We also tried the reduction of the nitro acid by Seidel's method, with sodium sulphide. Some amino acid was formed, but its separation and purification proved slow and troublesome.

The 4-aminophthalic acid was prepared readily by saponification of its dimethyl ester and also by hydrolysis of its imide. That the product thus obtained is really 4-aminophthalic acid was proven by its analysis and the analysis of its derivatives, by its reconversion into the characteristic dimethyl ester, by preparation therefrom of 4-chlorophthalic and of trimellitic acids, and by its other reactions. The anhydride and several salts were prepared. The imide was obtained by reduction of the nitro imide. Attempts to produce the imide from the ammonium salts or anhydride of the amino acid were unsuccessful, probably because the methods used involved heating to a temperature where deeper-seated changes occurred. When the dimethyl ester was heated to high temperatures with concentrated aqueous ammonia, a methylated imide resulted. Experiments were also conducted with the succinamic, phthalamic, ethoxalyl and phenyluramino derivatives of the dimethyl ester, and the urea was obtained from the ester and phosgene.

### Experimental.

#### *Preparation of 4-Amino-o-Phthalic Acid.*

(1) *By Reduction of the Nitro Acid with Tin (or Stannous Chloride) and Hydrochloric Acid.*—As just stated, our repetition of Miller's work confirmed his results. No carbon dioxide is lost during reduction, but on

<sup>1</sup> *Ber.*, **34**, 4352 (1901).

<sup>2</sup> *Monatsh.*, **26**, 1063 (1905).

<sup>3</sup> Baeyer, *Ber.*, **10**, 124 and 1079 (1877). Miller, *Ibid.*, **11**, 1191 (1878). Edinger, *J. prakt. Chem.* [2], **53**, 375 (1896). Ommert, *Ber.*, **34**, 3735 (1901). Bogert and Renshaw, *Loc. cit.*

de-tinning and evaporating the acid solution, carbon dioxide gradually escapes leaving only *m*-aminobenzoic acid. We succeeded also in demonstrating the presence of the aminophthalic acid in the solution at the close of the reduction. By adding an equal volume of concentrated hydrochloric acid to the reduced solution and lowering the temperature by means of a freezing mixture, a crop of crystals was obtained made up mostly of the aminophthalic acid but also carrying considerable tin, but on adding more hydrochloric acid to the mother-liquor from this first crop and further cooling, needles of fairly pure 4-aminophthalic acid were secured, which gave the characteristic 4-aminophthalanil when heated with aniline.

(2) *Reduction of the Nitro Acid with Sodium Sulphide*.—In repeating the work of Seidel,<sup>1</sup> we boiled 4-nitrophthalic acid for 15 hours with an alkaline solution of sodium sulphide and obtained 4-aminophthalic acid, unreduced nitro acid, sulphur, and a yellow powder not further investigated. Encountering considerable difficulty in separating the pure amino acid in good yield, the method was abandoned. In our previous article,<sup>1</sup> we called attention to the fact that Cohen and McCandlish,<sup>2</sup> in attempting to reduce the nitrophthalic ester with ammonium sulphide, failed to get a pure product, the amino ester being invariably contaminated with a yellow viscid oil.

(3) *From the Dimethyl Ester*.—Fifty grams of the ester dissolved in 200 cc. of alcohol were saponified by boiling for an hour with a solution of 13 grams (calculated, 11 grams) metallic sodium in 300 cc. alcohol. The sodium salt separated as a heavy cream-colored precipitate, which was filtered out, washed with alcohol, and dried at 90–100°. The yield was practically quantitative. An excess of sodium must be used, or the product is apt to be sticky and darkens rapidly in the air, due possibly to the presence of some acid sodium salt. The neutral sodium salt was dissolved in water and the free amino acid precipitated by addition of the calculated amount of hydrochloric acid. It separated as a cream-colored, granular precipitate. If the solution is dilute, the acid separates slowly in crystalline crusts. It was purified by recrystallization from water or alcohol, and gave the following analytical figures:

Found: C, 52.67, 52.86, 52.97 and 53.23; H, 4.02, 3.87 and 3.67; N, 7.96, 7.54 and 7.88. Calculated for  $C_8H_7O_4N$ : C, 53.01; H, 3.89; N, 7.75.

(4) *From the Imide*.—4-Nitrophthalimide was prepared by heating the acid ammonium salt of 4-nitrophthalic acid for some time at 190–200°, purifying the product by dissolving in acetone, reprecipitating with water, and recrystallizing from boiling water. It was reduced to the amino imide by the action of stannous chloride and hydrochloric acid,

<sup>1</sup> *Loc. cit.*

<sup>2</sup> *J. Chem. Soc.*, 87, 1269 (1905).

and this amino imide then boiled with concentrated aqueous ammonia, giving the neutral ammonium salt of 4-aminophthalic acid from which the acid itself was liberated by the action of hydrochloric acid.

*Properties of 4-Amino-o-phthalic Acid.*—As obtained by the above methods, the acid was generally a pale flesh-colored, granular powder. By slow crystallization from dilute solutions, it can be obtained in microscopic, colorless, glassy, irregular plates or lentil-shaped crystals, which gradually turn reddish in the air. Our best crystals were obtained from aqueous solutions containing a little acetic acid. It is soluble in acids, alkalis or organic bases; slightly soluble in boiling water or in 95 per cent. alcohol; very difficultly soluble in boiling benzene, acetone, amyl alcohol, chloroform, carbon tetrachloride, carbon bisulphide, nitrobenzene, ether or naphtha. Heated gradually, it loses water without melting, leaving a yellowish-gray infusible mass. Rapidly heated, it softens with rapid evolution of water, and then quickly solidifies to the infusible material. Boiled with hydrochloric acid, it gradually loses carbon dioxide and breaks down to *m*-aminobenzoic acid.

A small amount of the acid was boiled with excess of aniline, a slight excess of acetic acid then added, and the solution diluted. The crystals which separated proved to be 4-aminophthalanil, melting point  $204^{\circ}$  (uncor.).<sup>1</sup>

The conversion of the acid into its characteristic dimethyl ester (melting point  $84^{\circ}$ ),<sup>1</sup> was accomplished best by the method of Bogojavlenski,<sup>2</sup> the yield of ester being nearly quantitative.

By diazotizing the acid in presence of excess of hydrochloric acid, a chlorinated acid resulted, melting at  $150\text{--}151^{\circ}$  with loss of water. Claus and Dehne<sup>3</sup> give the melting point of 4-chlorophthalic acid as  $148^{\circ}$ , while Miersch<sup>4</sup> gives it as  $150\text{--}150.5^{\circ}$ .

In another experiment, the acid was diazotized and then added to a warm copper potassium cyanide solution. From the products of this reaction, there was separated a small amount of colorless, fleecy crystals, melting point  $204\text{--}207^{\circ}$ , which may have been impure trimellitic acid. The chief compound isolated, however, was yellow and granular. It was purified by solution in ether and re-precipitation with benzene, and microcrystalline crusts thus obtained, melting with loss of water at  $166^{\circ}$  (cor.). On analysis, it gave the following results:

Found: N, 6.6. Calculated for  $C_8H_7O_4N$ : N, 6.7.

Boiled with potassium hydroxide solution, ammonia was given off and the substance dissolved. This solution was acidified, extracted

<sup>1</sup> Bogert and Renshaw: *Loc. cit.*

<sup>2</sup> *Ber.*, **34**, 3344 (1901).

<sup>3</sup> *Ibid.*, **15**, 321 (1882).

<sup>4</sup> *Ibid.*, **25**, 2116 (1892).

with ether, and the ether evaporated. There remained a slightly yellowish solid, melting at 216–218° with evolution of water. As trimellitic acid melts at 216°, it seems probable that the compound described was its monamide,  $(4)\text{H}_2\text{NCO}\cdot\text{C}_6\text{H}_3(\text{COOH})_2(1,2)$ , produced by partial hydrolysis of the nitrile formed in the action of the diazo solution upon the copper cyanide. This monamide is very easily soluble in water or alcohol; moderately soluble in cold ethyl acetate, amyl valerate or ether; nearly insoluble in benzene, chloroform or carbon tetrachloride.

*Hydrochloride of 4-Aminophthalic Acid.*—The amino acid was dissolved in warm, very dilute hydrochloric acid, and an excess of concentrated hydrochloric acid added. On cooling, the hydrochloride separated in clusters of yellowish needles, soluble in water or alcohol, insoluble in ether. The crystals gradually lose hydrochloric acid on standing in the air, and decompose without melting when heated.

*Salts of 4-Aminophthalic Acid.*—Titration with standard alkali showed the acid to be bibasic.

*Sodium Salt.*—The preparation of this salt from the dimethyl ester is described above. It can be purified by crystallization from dilute alcohol, and then forms microscopic crystals of a pale cream color. It is easily soluble in water, but very difficultly soluble in alcohol. When moist, it darkens in the air. In one experiment, long, thin, lustrous needles were obtained, but they decomposed on filtering. It is probable that they carried some solvent of crystallization which was lost spontaneously on filtering.

*Potassium Salt.*—No good crystals were obtained either from aqueous or dilute alcoholic solutions. On concentration of the solutions, yellow amorphous crusts were left.

*Ammonium Salt.*—Failed to get good crystals. Pale, cream-colored amorphous crusts on evaporation.

*Calcium Salt.*—In concentrated solutions of the amino acid, solutions of calcium salts cause a yellow precipitate of calcium aminophthalate. Short, thick prisms (from water), which darken in the air.

*Barium Salt.*—Precipitates on adding a solution of a barium salt to one of the amino acid. It is difficultly soluble in water, and crystallizes from it in small flakes.

Ba found, 42.79. Calculated for  $\text{C}_8\text{H}_5\text{O}_4\text{NBa}$ : Ba, 42.43.

*Nickel Salt.*—Precipitates as a dirty green powder when nickelous salts are added to an aqueous solution of the amino acid. It dissolves with difficulty in hot water, giving a grass-green solution.

*Copper Salt.*—Yellowish green precipitate, only slightly soluble in hot water, but in contact with water it slowly changes to dark green nodules of microscopic crystals.

*Lead Salt.*—Insoluble, pale salmon-colored precipitate.

*Silver Salt.*—The amino acid was dissolved in a slight excess of ammonia, an aqueous solution of silver nitrate added, and then nitric acid to acid reaction. The silver salt separated as a cream-colored curdy precipitate, which was thoroughly washed, dried, and analyzed:

Found: Ag, 54.5. Calculated for  $C_8H_5O_4NAg_2$ : Ag, 54.64.

It is slightly soluble in hot water, and can be obtained in small thin plates by crystallizing from this solvent. It soon darkens in the light.

*Mercuric Chloride Double Salt.*—A solution of mercuric nitrate was added to an aqueous solution of the amino acid containing hydrochloric acid. The whole was warmed and then allowed to cool gradually. After some time, clusters of colorless, prismatic crystals separated. These crystals also darken rapidly in the light.

*Other Derivatives of 4-Aminophthalic Acid.*

*Action of Heat on Dimethyl 4-Aminophthalate.*—When the ester was heated at 180–200°, methyl alcohol was split off, and a slight odor resembling that of methylamine was noted. If the heating was continued long enough, a vitreous brown melt resulted. It seems probable that interaction occurs between the ester groups of some of the molecules and the amino group of others, with formation of complex condensation products.

*4-Aminophthalic Anhydride*,  $H_2N.C_6H_3 \begin{array}{c} \diagup CO \\ \diagdown CO \end{array} O$ .—The acid was heated

in an air bath at 180–200° for two hours, and was then treated with water, boiling alcohol, and boiling ether, dried at 175° for an hour, re-extracted, dried at 110°, and analyzed:

Found: N, 8.40 and 8.44. Calculated for  $C_8H_5O_3N$ : N, 8.58.

It is a pale salmon-colored solid, only slightly soluble in the ordinary neutral solvents. In cold potassium hydroxide solution, it dissolves slowly in the cold and, on acidifying this solution, 4-aminophthalic acid is recovered. It does not melt, but gives off more water at higher temperatures, perhaps with formation of a polymolecular imide, and finally carbonizes.

*4-Acetaminophthalic Anhydride*,  $CH_3CONH.C_6H_3 \begin{array}{c} \diagup CO \\ \diagdown CO \end{array} O$ .—This was

prepared direct from the amino acid by the action of acetic anhydride or acetyl chloride, and purified by recrystallization from a mixture of acetyl chloride and ethyl acetate. Microscopic needles, melting point 206–207° (cor.).

Found: N, 6.82 and 6.88. Calculated for  $C_{10}H_7O_4N$ : N, 6.84.

It is soluble in acetone, alcohol, ethyl acetate or amyl valerate; slightly soluble in ether. On standing, it undergoes some change by which a portion becomes insoluble in the above solvents.

In this acetylation, another product was encountered, melting point  $134^{\circ}$  (uncor.) with loss of water. Even on drying at  $80-90^{\circ}$ , it changed almost wholly to the anhydride. Whether it was the acetamino acid or not we are unable to state, as the amount available was insufficient for identification.

*4-Aminophthalimide*.—The preparation of the imide from the amino acid proved more troublesome than expected. When the dimethyl ester was heated with aqueous or alcoholic ammonia under pressure, methylated products resulted. Nor could a good yield of imide be obtained by heating the neutral or acid ammonium salts, or by passing ammonia over the anhydride. The only satisfactory method proved to be the reduction of the corresponding nitrophthalimide with stannous chloride and hydrochloric acid.

Five grams of the nitro imide were added to a solution of 20 grams stannous chloride in 150 cc. concentrated hydrochloric acid and 50 cc. water, stirring gently with a turbine. When all the nitro imide was dissolved, twice the volume of concentrated hydrochloric acid was added and the solution well cooled. The supernatant acid liquor was then decanted from the cream-colored precipitate and the latter shaken up with water, to hydrolyze the hydrochloride. The yellow substance obtained was purified by crystallization from water and gave long, yellow needles, which began to sublime at about  $277^{\circ}$ , gradually softened and finally melted at  $294^{\circ}$  (cor.).

Found: N, 17.48. Calculated for  $C_8H_6O_2N_2$ : N, 17.33.

The pure substance forms golden yellow needles, very slightly soluble in cold water, ether, chloroform or carbon bisulphide; moderately soluble in the same solvents at their boiling points or in boiling benzene; easily soluble in alcohol or acetone; practically insoluble in petroleum ether. Its *hydrochloride* is gray and crystalline.

*4-Aminophthalmethyylimide*,  $H_2N.C_6H_3 \begin{matrix} \diagup CO \\ \diagdown CO \end{matrix} NCH_3$ .—In an attempt to prepare the simple imide from the dimethyl ester and ammonia, 5 grams of the ester were heated for three hours in a sealed tube, at  $280-290^{\circ}$ , with 20 cc. of concentrated aqueous ammonia. On opening the tube, an odor resembling that of methylamine was noted and the presence of an inflammable gas burning with a blue flame. The solution, containing some canary-yellow crystals, was concentrated, cooled, and the separated crystals purified by recrystallization from very dilute ammonia. The purified substance melted at  $242-243^{\circ}$  (cor.).

Found: N, 15.9, 16.09, 16.09 and 16.06. Calculated for  $C_9H_8O_2N_2$ : N, 15.95.

The compound is readily soluble in alcohol, acetone or hot ethyl acetate; moderately soluble in boiling water, ether or benzene; practically in-

soluble in petroleum ether; its aqueous solution darkens on concentration. Under diminished pressure, it can be sublimed without much decomposition.

To ascertain its structure, a small amount of the substance was distilled down twice with excess of strong potassium hydroxide solution, the distillate being caught in dilute acetic acid. On adding excess of potassium hydroxide to this distillate, a strong odor of methylamine was observed. The material left in the distilling flask was treated twice with warm absolute alcohol to remove excess of potassium hydroxide, the residue then dissolved in water and the solution acidified. The acid which separated gave 4-aminophthalanil when boiled with aniline.

In further corroboration of the structure assigned, the same substance was obtained by reduction of 4-nitrophthalthmethylimide with stannous chloride and hydrochloric acid.

*Hydrochloride*.—Plates, hydrolyzed by water.

The formation of this imide presents a rather interesting case of methylation. It appears to be due to some of the methyl alcohol split off in the first phase of the reaction. It has often been observed<sup>1</sup> that ether acids or their salts on heating yield some ester of the ether acid, and acid esters of bibasic acids occasionally<sup>2</sup> give some neutral ester when heated sufficiently, but the authors have not met in the literature any case quite like the formation of the above methylated imide.

*4-Nitrophthalthmethylimide*,  $\text{O}_2\text{NC}_6\text{H}_3 \begin{array}{c} \diagup \text{CO} \\ \diagdown \text{CO} \end{array} \text{NCH}_3$ .—The acid methyl-

amine salt of 4-nitrophthalic acid was heated at  $175\text{--}180^\circ$  for two hours, and the crude melt purified by treating with bone black and crystallizing from alcohol. Long, white needles were thus obtained, melting at  $179\text{--}180^\circ$  (cor.), readily soluble in acetone, ethyl acetate, chloroform or hot alcohol; moderately soluble in benzene, ether or boiling water.

Found: N, 13.67. Calculated for  $\text{C}_6\text{H}_4\text{O}_4\text{N}_2$ : N, 13.63.

*4-Aminophthalanil*.—As noted above, this anil can be prepared readily by heating the free amino acid with aniline. As previously reported, it melts at  $205.5^\circ$  (cor.).<sup>3</sup>

*Di-[dimethyl 4-Aminophthalate] Urea*,  $\text{CO}(\text{NHC}_6\text{H}_3(\text{COOCH}_3)_2)_2$ .—Dimethyl 4-phenyluraminophthalate,  $\text{C}_6\text{H}_5\text{NHCONHC}_6\text{H}_3(\text{COOCH}_3)_2$ ,<sup>3</sup> when gradually heated, does not split smoothly into the urea and carbanilide expected,<sup>4</sup> but undergoes more extensive decomposition.

<sup>1</sup> Heintz, *Jahresb.*, 1861, 448. Pollak and Goldstein, *Ann.*, 351, 161 (1907). Goldschmiedt and Herzig, *Monatsh.*, 3, 126 (1882). Heinisch, *Ibid.*, 14, 455 (1893) and 15, 235 (1894). Arnstein, *Ibid.*, 15, 295 (1894). Hübner, *Ibid.*, 15, 720 (1894).

<sup>2</sup> Malaguti, *Ann. chim.* [2], 64, 152 (1838).

<sup>3</sup> Bogert and Renshaw, *Loc. cit.*

<sup>4</sup> Compare Bogert and Beans, *THIS JOURNAL*, 26, 466 (1904). Bogert and Chambers, *Ibid.*, 28, 210 (1906).

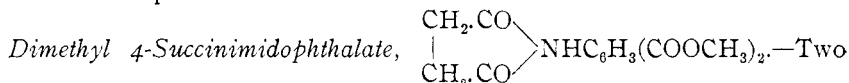


The urea was, however, produced by treating a pyridine solution of the dimethyl ester with a toluene solution of phosgene. Upon bringing these solutions together, a yellow precipitate immediately separated, subsequently dissolving to a cherry-red solution, the color changing to yellow on further heating. The solution was boiled, allowed to cool, and poured into a large volume of water. The yellow toluene layer was separated, washed, diluted with alcohol, treated with bone-black and cooled thoroughly. Short needles crystallized out which, after purification, showed a melting point of  $213-214^{\circ}$  (cor.).

Found: N, 6.47. Calculated for  $C_{21}H_{20}O_6N_2$ : N, 6.30.

The pure compound forms colorless prisms, soluble in boiling water, alcohol or acetone, but only slightly soluble in hot benzene or in chloroform.

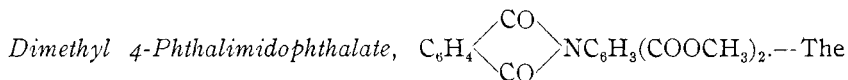
*Dimethyl Ethoxalyl-4-aminophthalate*.—The melting point of this compound, given in our previous paper as  $121.5^{\circ}$  (cor.), should be changed to  $126^{\circ}$  (cor.). When it was heated for an hour at  $215^{\circ}$ , it was for the most part unchanged. There was no evidence of the formation of any oxalimido compound.



grams of the succinamic acid of dimethyl 4-aminophthalate,<sup>1</sup>  $\text{HOOCCH}_2\text{CONHC}_6\text{H}_3(\text{COOCH}_3)_2$ , were heated at  $210-220^{\circ}$  for two hours. The resulting brownish melt was extracted with boiling water, the solution treated with bone-black and concentrated. Large needles separated on cooling which, after recrystallization from water, showed a melting point of  $153.4^{\circ}$  (cor.).

Found: N, 5.16 and 5.03. Calculated for  $C_{14}H_{13}O_6N$ : N, 4.81.

The compound crystallizes in colorless prisms or needles; soluble in alcohol, benzene, chloroform, boiling water or hot glacial acetic acid; nearly insoluble in cold water or in cold acetic acid.



corresponding phthalamic acid<sup>1</sup> was heated at  $180-200^{\circ}$  until the copious evolution of water which began at its melting point ( $166-167^{\circ}$ ) had ceased. The melt was dissolved in alcohol, treated with bone-black, and concentrated to crystals. Long needles were obtained, melting at  $174^{\circ}$  (cor.).

Found: N, 4.41 and 4.25. Calculated for  $C_{18}H_{13}O_6N$ : N, 4.1.

The pure substance forms colorless needles or prisms; soluble in benzene,

<sup>1</sup> Bogert and Renshaw, *Loc. cit.*

chloroform, acetone or hot alcohol; very difficultly soluble in boiling water, carbon bisulphide, ether, petroleum ether, dilute acid or alkalis.

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NEW YORK CITY, N. Y., April, 1908.

[CONTRIBUTIONS FROM THE CHEMICAL LABORATORY OF HARVARD COLLEGE.]

## METHYL ETHYL ISOBUTYL METHANE.

BY LATHAM CLARKE.

Received May 7, 1908.

In continuing the research on the octanes undertaken some time ago in this laboratory,<sup>1</sup> the synthesis of methylethyl isobutyl methane,  $\begin{matrix} \text{CH}_3 \\ \text{C}_2\text{H}_5 \end{matrix} \text{CH} - \text{CH}_2 - \text{CH}(\text{CH}_3)_2$ , or 2-4-dimethyl hexane has been accomplished.

In the preparation of this hydrocarbon the two following series of reactions promised a pure product and both were therefore used.

*First Method.*—From isopropyl acetacetic ester by saponification methyl isobutyl ketone was obtained. This, when treated with ethyl magnesium bromide, yielded 2-4-methyl-4-hexanol,  $\text{CH}_3\text{CH}_2 - \underset{\text{CH}_3}{\text{C}}(\text{OH}) - \underset{\text{CH}_3}{\text{CH}_2}\text{CH} - \text{CH}_3$ .

This carbinol, on transforming into the corresponding iodide and reducing, gave the desired octane.

These reactions are herewith summarized:

$\text{CH}_3\text{COCH} - \text{CO}_2\text{C}_2\text{H}_5$ , isopropyl acetacetic ester  $\xrightarrow{\quad}$

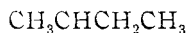
$\begin{matrix} | \\ \text{CH}(\text{CH}_3)_2 \end{matrix}$   
 $\text{CH}_3\text{COCH}_2 - \text{CH}(\text{CH}_3)_2$ , methylisobutyl ketone  $\xrightarrow{\quad}$

$\text{CH}_3\text{CH}_2\text{C}(\text{OH}) - \text{CH}_2\text{CH}(\text{CH}_3)_2$ , 2-4-methyl-4-hexanol  $\xrightarrow{\quad}$

$\begin{matrix} | \\ \text{CH}_3 \end{matrix}$   
 $\text{CH}_3\text{CH}_2 - \text{C} - (\text{I}) - \text{CH}_2\text{CH}(\text{CH}_3)_2$ , 2-4-methyl-4-iodohexane  $\xrightarrow{\quad}$

$\begin{matrix} | \\ \text{CH}_3 \end{matrix}$   
 $\text{CH}_3\text{CH}_2 - \text{CH} - \text{CH}_2\text{CH}(\text{CH}_3)_2$ , methyl ethyl isobutyl methane or 2-4-dimethyl hexane.

*Second Method.*—Secondary butyl alcohol was converted into the corresponding iodide and made to react with sodium acetacetic ester, thus forming ethyl secondary butyl acetacetate,  $\text{CH}_3\text{COCHCO}_2\text{C}_2\text{H}_5$ .



<sup>1</sup> Preliminary notice. *Ber.*, 40, 352.