The theoretical value was used in the test analyses given below, which indicate very satisfactory results for the method.

No.	Ni steel. Gram.	cc. KCN.	Per cent. nickel.	Ni by other methods.
1A	0.5000	6.70	3.70	3.65
2A	0.5000	6.62	3.67	3.65
3A	0.5000	6.60	3.66	3.65
1B	0.5000	6.25	3.46	3.47
2B	0.5000	6.26	3.48	3.47

SHEFFIELD LABORATORY, NEW HAVEN, CONN.

[CONTRIBUTIONS FROM THE SHEFFIELD LABORATORY OF YALE UNIVERSITY.]

RESEARCHES ON AMINES: ALKYLATIONS WITH DIMETHYLSULPHATE. SYNTHESIS OF DIMETHYLPHENYLETHYLAMINE.

(THIRD PAPER.)

BY TREAT B. JOHNSON AND HERBERT H. GUEST.

Received March 23, 1910.

Contents.—1. Historical. 2. Purpose of Investigation and Discussion of Results. 3. Experimental Part.

1. Historical.

That dialkylsulphates (dimethyl- and diethylsulphates) can be used in place of the corresponding halides for the alkylation of amines has been known for a long time. Dumas and Peligot,[1] in 1835, examined the behavior of dimethylsulphate towards ammonia and observed the formation of methylalcohol and methylammonium sulphate (Sulfomethylan). Strecker[2] repeated this experiment and also investigated the action of diethylsulphate on ammonia. He found that the reactions were not as simple as assumed by Dumas and Peligot and obtained, with diethylsulphate, the ammonium salt of an acid, $C_{16}H_{23}NO_4.4SO_3 + NH_3$ (äthylaminschwefelsäure Ammoniak), from which he prepared ethylamine by decomposition with alkali.

Babo[3] examined the action of dimethylsulphate (Schwefelsaures Methyloxyd) on aniline and showed that it alkylated smoothly giving monomethylaniline. He also observed that quinoline and nicotine reacted with this reagent and diethylsulphate giving crystalline addition products (quaternary compounds?).

The study of the action of these sulphates on amines received no further attention, apparently, until 1880 when a paper by Claesson and Lundvall[4] appeared, in which they describe their behavior towards ammonia and several aliphatic and aromatic bases. They repeated the work of Strecker and observed that diethylsulphate reacted with ammonia giving not only

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[1] *Ann. chim. phys.*, 58, 32.

[2] *Ann.*, 75, 46.

[3] *J. pr. Chem.*, [1] 72, 84 (1857); *Chem. Centr.*, 218 (1858).

[4] *Ber.*, 13, 1700.

ethylamine, but also the quaternary salt $(C_2H_5)_4N.SO_4C_2H_5$. Quaternary salts were also obtained by alkylation of diethylamine, dimethylaniline and tribenzylamine with dimethylsulphate. They write: "Die Reaktion zwischen Ammoniak und Methylsulfat ist somit eine rein additionelle. Sie verläuft nach folgender Gleichung:

$$CH_3OSO_2OCH_3 + NH_3 = CH_3OSO_2ONH_3.CH_3."$$

The usefulness of dimethylsulphate as an alkylating agent for amines was later greatly enhanced by the work of Ullmann and his co-workers.[1] They showed that it not only reacted smoothly with organic bases (in ether, chloroform and benzene), but also that it can be employed successfully for the alkylation of cyclic amines, *viz.*: quinolines, aminonaphthacridines, phenylacridines, diaminoacridines and aminophenazines. They write:[2] "Die Resulte übersehen lassen, dass Dimethylsulfat in allen Fällen das Iodmethyl ersetzen kann, aber meistens noch bedeutend rascher und besser als dieses reagirt." Ullmann's[3] interpretation of the reactions between amines and dimethylsulphate is summarized in his own words—"Dieselbe verläuft nämlich nicht, wie Claesson und Lundvall augegeben,—Es entsteht also das methylschwefelsäure primäre Amin und die entsprechende secundäre Base."

$$(CH_3)_2SO_4 + 2RNH_2 = RNH_2.H.CH_3SO_4 + RNHCH_3.$$

Decker and his students[4] have used the alkylsulphates for the preparation of quaternary derivatives of cyclic bases. For example, they were unable to obtain quaternary compounds of several quinolines by addition of methyliodide, while, on the other hand, dimethylsulphate reacted quantitatively giving the corresponding quaternary alkyl sulphates. Methyldiphenylamine reacted smoothly with dimethylsulphate at 140–150° giving the quaternary compound $(C_6H_5)_2(CH_3)_2NSO_4CH_3$[5] while no addition took place with methyliodide under the same conditions.

The action of dimethylsulphate on the glyoxaline ring was studied by Pinner.[6] He examined its behavior towards diphenylglyoxaline I, and triphenylglyoxaline (Lophine) II, but did not observe the formation of nitrogen methyl derivatives. Lophine reacted abnormally with the sulphate giving a characteristic double compound, $C_{21}H_{16}N_2.(CH_3)_2SO_4.2H_2O$, having the properties of a salt. Pinner remarks that the sulphate acts in this case as a weak acid and that the compound has not the possible structure of a quaternary compound III (Methylschwefelsaures Methyl-

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[1] Ullmann and Naef, *Ber.*, 33, 2470 (1900); Ullmann and Wenner, *Ibid.*, 33, 2476; Ullmann and Marié, *Ibid.*, 34, 4307 (1901); Ullmann, *Ann.*, 327, 104 (1903).

[2] Ullmann and Wenner, *Loc. cit.*

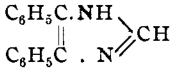
[3] *Ann.*, 327, 107.

[4] *Ber.*, 36, 261 (1903); 38, 1147, 2493; Decker and Schenck, *Ibid.*, 39, 748; Schmid and Decker, *Ibid.*, 39, 933 (1906).

[5] Gadomska and Decker, *Ber.*, 36, 2487 (1903).

[6] *Ber.*, 35, 4141 (1902).

lophin). He writes: "Es ist nicht ohne Interesse, das Verhalten von Methylsulfat anderen Basen gegenüber zu untersuchen."



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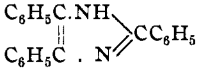

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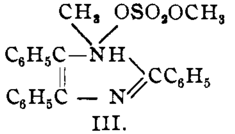

III.

Bamberger[1] employed dimethylsulphate for the preparation of *o*-monomethyl- and *o*-dimethylaminobenzaldehydes from *o*-aminobenzaldehyde and also later for the alkylation of mesidine to monomethyl- and dimethylmesidines.[2] This reagent has also been used successfully for the alkylation of amino compounds by Johnston,[3] Baeyer,[4] Willstätter and Kahn,[5] Weil,[6] Smith,[7] Burmann,[8] Frohlich,[9] and Houben and Brassert.[10]

In no case, so far as the writer is aware, has it been observed that an amine can react with dimethylsulphate, in a similar manner as with an aliphatic ester, giving an amide of sulphuric acid. It is interesting to note in this connection that recent attempts by Ephraim and Gurewitch[11] to prepare sulfamide $SO_2(NH_2)_2$ from dimethylsulphate by action of ammonia, in alcohol solution and in liquid form, were unsuccessful. They reacted, under both conditions, with formation of methylamine according to the following equation:

$$SO_2(OCH_3)_2 + 2NH_3 = CH_3OSO_2ONH_4 + NHCH_3.$$

2. Purpose of Investigation and Discussion of Results.

The work described in this paper was undertaken with the object of determining the behavior of dimethylsulphate towards some aromatic β-amines.

Any methods, by which the nitrogen alkyl derivatives of phenylethylamine IV, or *p*-hydroxyphenylethylamine V, can be obtained easily are of value, on account of the interest, at the present time, of compounds

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[1] *Ber.*, **37**, 966 (1904).

[2] Bamberger and Rudolf, *Ibid.*, **39**, 4285 (1906).

[3] *Proc. Chem. Soc.*, **21**, 156; *Chem. Centr.*, **1905**, II, 44; *Proc. Roy. Soc.* (London), **78**, 82; *Chem. Centr.*, **1906**, II, 1006.

[4] *Ann.*, **354**, 152.

[5] *Ber.*, **37**, 408 (1904).

[6] *Monatsh.*, **29**, 875.

[7] *J. Chem. Soc.*, **89**, 1505 (1906).

[8] *Bull. soc. chim.*, [3] **35**, 801 (1906).

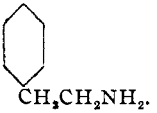
[9] *Ber.*, **42**, 1561 (1909). For further works on alkylation of amines with alkylsulphates see: D. R. P. 79703 (1895). D. R. P. 102634. *Chem. Centr.*, **1899**, II, 408 (Merck). D. R. P. 131758. *Ibid.*, **1902**, I, 1385. D. R. P. 134176. *Ibid.*, **1902**, II, 775 (Farbenfabriken vorm. Friedr. Bayer & Co.); Berger, *Diss. Leipzig* (1904); Feuerlein, *Diss. Zurich* (1907).

[10] *Ber.*, **43**, 206.

[11] *Ibid.*, **43**, 139 (1910).

of this character to pharmacologists. Of all the nitrogen alkyl derivatives of phenylethylamine, dimethylphenylethylamine, VII, is probably the the most interesting because of its close structural relationship to the naturally occurring alkaloid *hordenine*, VIII (dimethyl-*p*-hydroxyphenylethylamine). It seemed desirable therefore, to the writer, to determine whether this base, VII, can be synthesized by direct alkylation of phenylethylamine. Previous attempts to prepare it by alkylation of the latter with methyliodide have been unsuccessful.

Johnson and Guest[1] showed in a paper from this laboratory that methyliodide reacts with phenylethylamine giving the hydriodide of the unaltered base and the quaternary derivative—*trimethyl-phenylethylammonium-iodide.* No matter what proportion of the methyliodide was used, they obtained no evidence of the formation of monomethyl- or dimethylphenylethylamines, VI and VII. This observation was later confirmed by Barger.[2]



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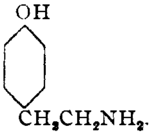

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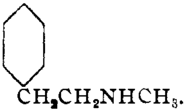

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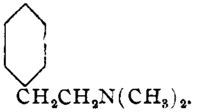

VII.

VIII.

We now find that this base, VII, can be prepared from phenylethylamine by alkylation with dimethylsulphate. Several negative experiments, however, were performed before we finally succeeded in obtaining conditions favorable for its formation. All attempts to alkylate in aqueous solution, in the presence of alkali, were unsuccessful. The action of dimethylsulphate, in ether, was also investigated, but the results were similar to those obtained in our alkylation experiments with methyliodide. The products of the reaction were the phenylethylamine salt of methylsulphuric acid and a hydroscopic salt having the properties of a quaternary derivative. Conversion into the tertiary base was finally accomplished by alkylation, in methyl alcohol, in the presence of sodium methylate. In this manner a good yield of the base was obtained, which boiled at 200–204° at ordinary pressure.

This same amine (b. 198–202°) has also recently been prepared by Barger[3] by heating phenylethylchloride with dimethylamine, but so little

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[1] *Am. Chem. J.*, **42**, 340.

[2] *J. Chem. Soc.* (London), **95**, 2194.

[3] *Loc. cit.*

material was obtained by him that it was not analyzed nor well characterized. Since he showed that the base gives, by nitration at —10°, a good yield of the paranitro derivative IX (60 per cent.), which can be converted into a base identical with *hordenine*, our synthesis of the amine VII therefore offers a method of preparing *hordenine* directly from phenylethylamine.

$$C_6H_5CH_2CH_2NH_2 \longrightarrow C_6H_5CH_2CH_2N(CH_3)_2 \longrightarrow \underset{\text{IX.}}{NO_2C_6H_4CH_2CH_2N(CH_3)_2} \longrightarrow HOC_6H_5CH_2CH_2N(CH_3)_2$$

The interesting behavior of phenylethylamine towards dimethylsulphate led us to examine also the action of this reagent on *p*-nitrophenylethylamine.[1] To our surprise, this base underwent no alkylation, in methyl alcohol, in the presence of sodium methylate and practically 90 per cent. of the amine used was recovered unaltered. It was identified by its hydrochloride, and on reduction was converted smoothly into *p*-aminophenylethylamine.[2]

This difference between phenylethylamine and *p*-nitrophenylethylamine, in their behavior towards dimethylsulphate, is probably due to the fact that one is a much stronger base than the other. Phenylethylamine, being the most basic, adds dimethylsulphate at once, and undergoes alkylation before the sulphate is decomposed by the sodium methylate. On the other hand, *p*-nitrophenylethylamine, which is the weaker base on account of the negative influence of the *p*-nitro group, has a much less tendency to add the sulphate, under the conditions of the experiment; consequently the latter is completely decomposed by the sodium methylate and the amine is recovered unaltered. Dimethyl sulphate would be expected to react readily with sodium methylate, in a similar manner as with methyliodide, giving dimethyl ether and the sodium salt of methylsulphuric acid or sodium sulphate,

$$CH_3OSO_2OCH_3 + NaOCH_3 = CH_3OSO_2ONa + (CH_3)_2O,$$

or

$$CH_3OSO_2OCH_3 + 2NaOCH_3 = Na_2SO_4 + 2(CH_3)_2O.$$

That our assumption is correct is supported by the fact that the odor of dimethyl ether was apparent during the reaction, and also by a previous observation of Nef.[3] He showed, for example, that dimethylsulphate is decomposed practically quantitatively when dissolved in a cold methyl alcohol solution of potassium hydroxide, giving dimethyl ether and potassium sulphate.

Attempts to prepare secondary and tertiary amines from *p*-nitrophenylethylamine by alkylation with methyliodide were also unsuccessful.

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[1] Johnson and Guest, *Am. Chem. J.*, **43**.

[2] Johnson and Guest, *Loc. cit.*

[3] *Ann.*, **309**, 186 (1899).

They reacted at 100°, in methyl alcohol, giving the hydriodide of the unaltered base and *trimethyl-p-nitrophenylethylammonium iodide.*

The writers[1] have shown that acetyl-*p*-nitrophenylethylamine can be obtained in good yield by nitration of acetylphenylethylamine. We now find that the corresponding methyl derivative of this nitro amide, XI, can be prepared, in a similar manner, by nitration of acetylmethylphenylethylamine, X. It was converted quantitatively into the unknown *p*-nitrophenylethylmethylamine, XII, by hydrolysis with acids.

$$C_6H_5CH_2CH_2NH_2 \longrightarrow C_6H_5CH_2CH_2NHCH_3 \longrightarrow$$

$$\underset{\text{X.}}{C_6H_5CH_2CH_2N(CH_3)COCH_3} \longrightarrow \underset{\text{XI.}}{NO_2C_6H_4CH_2CH_2N(CH_3)COCH_3} \longrightarrow$$

$$\underset{\text{XII.}}{NO_2C_6H_4CH_2CH_2NHCH_3.}$$

3. Experimental Part.

Action of Dimethylsulphate on Phenylethylamine in Ether.—Five grams of the amine were dissolved in ether and 20 grams of the sulphate (8 mols.) added slowly to the solution. There was an immediate reaction with evolution of heat and about 10 grams of a colorless crystalline salt separated. After allowing to stand for an hour, this was filtered off and the ether filtrate allowed to evaporate. We obtained an oil (mostly unaltered dimethylsulphate) to which was added an excess of alkali and then subjected to steam distillation. No bases were carried over by the steam. A portion of the material, insoluble in ether, was purified by dissolving in alcohol and then precipitating by dilution with ether. Glistening plates separated and melted at 75–77° to an oil. A nitrogen determination indicated that the substance was the *phenylethylammonium salt of methylsulphuric acid,* $C_6H_5CH_2CH_2NH_3.SO_4CH_3$.

Calculated for $C_9H_{15}O_4NS$: N, 6.0; found: N, 5.55.

The remainder of the salt was shaken with an excess of ether and in presence of a strong aqueous solution of sodium hydroxide. A crystalline product remained undissolved by this treatment. It was soluble in cold water and alcohol and could be warmed in sodium hydroxide solution without decomposition. The compound was very hydroscopic, contained sulphur and decomposed from 100–110° with effervescence. Its chemical behavior indicated that it was a quaternary salt.

Phenylisothiocyanate was added to the ether solution above and the ether allowed to evaporate in the air. Beautiful prisms of 1-phenyl-2-phenylethylthiourea finally separated and melted, after one crystallization from alcohol, at 106°. A mixture of this compound and some of the pure thiourea prepared from phenylethylamine melted at the same temperature.

Dimethylphenylethylamine, $C_6H_5CH_2CH_2N(CH_3)_2$.—Eight and four-tenths grams of metallic sodium (3 at.) were dissolved in 135 cc. of methyl

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[1] *Loc. cit.*

alcohol and 14.5 grams of phenylethylamine added to the solution. Kahlbaum's dimethylsulphate (46 grams) was then added, in small portions, when there was a violent reaction with evolution of heat and separation of a gelatinous salt. After the final addition of dimethylsulphate, 50 cc. of methyl alcohol were added and the mixture heated on the steam bath for about 5 hours. It was then acidified with hydrochloric acid and evaporated to dryness to remove the excess of alcohol and acid. In order to separate the base, the hydrochloride was decomposed with an excess of sodium hydroxide and the bases distilled with steam and dissolved in hydrochloric acid. On evaporating to dryness a hydroscopic salt was obtained, which was dissolved in 75–100 cc. of cold water and treated with an excess of potassium nitrite, for about 10 minutes, to remove any primary and secondary amines. An excess of alkali was then added and the tertiary amine extracted with ether and dried over potassium hydroxide. It is a strong base which absorbs carbon dioxide from the air and boils at 200–205° at ordinary pressure. The yield was good.

Calculated for $C_{10}H_{15}N$: N, 9.40; found: N, 9.38.

Platinum Salt.—Crystallizes from water in hexagonal tables which decompose at 221°. A mixture of this salt and the corresponding salt of methylphenylethylamine[1] (m. 212°) melted below 207°.

Hydrochloride, $C_6H_5CH_2CH_2N(CH_3)_2.HCl$.—This salt was prepared by dissolving the base in dilute hydrochloric acid and then allowing the solution to evaporate in a vacuum over potassium hydroxide. The salt separated under these conditions in colorless plates, which melted at 205° to an oil. It decomposed with effervescence when heated above 270°.

Acetylmethylphenylethylamine, $C_6H_5CH_2CH_2N(CH_3)COCH_3$.—This amide was prepared by carefully adding 15 grams of freshly distilled thioacetic acid to 19 grams of methylphenylethylamine[1] and then heating at 210° for 1–2 hours to complete the reaction. The amide was a dark-colored oil, which did not solidify after standing at ordinary temperature for several hours. It was used for the following preparation without further purification.

Acetylmethyl - p - nitrophenylethylamine, (*p*) $NO_2C_6H_4CH_2CH_2N(CH_3)COCH_3$.—This compound was prepared by dissolving 25 grams of acetylmethylphenylethylamine in 85 cc. of nitric acid (sp. gr. 1.51). The temperature was not allowed to rise above 5° during the nitration. After allowing to stand for a few minutes the solution was then diluted with ice water and the nitric acid neutralized with ammonia when the amide separated as an oil. This was extracted with ether and the ether solution allowed to evaporate spontaneously when the amide finally

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[1] Johnson and Guest, *Loc. cit.*

solidified. More separated from the aqueous filtrate on standing. The crude substance melted at 90–94°.

The amide is very soluble in ethyl acetate, ethyl alcohol, chloroform and benzene. It was purified for analysis by several recrystallizations from ethyl acetate and a mixture of petroleum ether and benzene. It melted at 100–101° to a clear oil without effervescence (Kjeldahl):

Calculated for $C_{11}H_{14}O_3N_2$: N, 12.6; found: N, 12.10.

Oxidation of Acetylmethyl-p-nitrophenylethylamine with Potassium Dichromate.—About 0.9 gram of this amide and 3.2 grams of potassium dichromate were dissolved in 6.5 cc. of concentrated sulphuric acid and the solution heated at 60° for about 10–12 hours. A crystalline acid was obtained, which crystallized from hot water in prismatic crystals, and melted, after purification, at 234°. It was identified as paranitrobenzoic acid. A mixture of our acid and paranitrobenzoic acid melted at the same temperature.

Methyl-p-nitrophenylethylamine, (*p*) $NO_2C_6H_4CH_2CH_2NH(CH_3)$.—This amine was obtained, in the form of its hydrobromide, when the above acetyl derivative was digested with hydrobromic acid. The base separated as a heavy, yellow oil when sodium hydroxide was added to an aqueous solution of the hydrobromide.

1-Phenyl - 2,2 - methyl - p - nitrophenylethylthiourea, (*p*) $NO_2C_6H_4CH_2CH_2N(CH_3)CSNHC_6H_5$.—This thiourea was prepared by the action of phenylisothiocyanate on the above methyl-*p*-nitrophenylethylamine. It crystallizes from 95 per cent. alcohol in plates, which melt at 137–138°. A mixture of this thiourea and 1-phenyl-2-paranitrophenylethylthiourea[1] melted at 109–115° (Kjeldahl):

Calculated for $C_{16}H_{17}O_2N_3S$: N, 13.3; found: N, 12.8.

Action of Dimethylsulphate on Paranitrophenylethylamine, $NO_2C_6H_4CH_2CH_2NH_2$.—Nine and two-tenths grams of the hydrochloride of *p*-nitrophenylethylamine[1] were dissolved in 50 cc. of methyl alcohol containing 3.7 grams of sodium. Fourteen and three-tenths grams of dimethylsulphate, boiling at 104–110° at 28–30 mm., were then added slowly to the cooled solution by means of a dropping funnel. There was an immediate reaction with evolution of much heat. After the addition of dimethylsulphate the mixture was heated to boiling, allowed to stand for 2.5 hours, acidified with an excess of hydrochloric acid and finally concentrated on the steam bath. An excess of alkali was then added when unaltered *p*-nitrophenylethylamine separated. This was extracted with ether and dried over potassium carbonate. The yield was 6.0 grams. A theoretical yield of unaltered *p*-nitrophenylethylamine would be 7.0 grams. The hydrochloride melted at 213–214°.[1]

Reduction of the Nitrophenylethylamine to Paraaminophenylethylamine,[1]

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[1] Johnson and Guest, *Loc. cit.*

$NH_2C_6H_4CH_2CH_2NH_2$.—The 6.0 grams of crude base were dissolved in a mixture of 30 cc. of 95 per cent. alcohol and 30 cc. of concentrated hydrochloric acid, and reduced for 8–10 hours with 8.5 grams of tin. We obtained a clear solution of the tin double salt which was evaporated to remove the excess of hydrochloric acid. The salt was then dissolved in cold water, the tin precipitated by hydrogen sulphide and the solution evaporated to dryness. A hydroscopic salt was obtained which was insoluble in cold alcohol and ethyl acetate but extremely soluble in cold water. It dissolved in 95 per cent. alcohol and was precipitated by addition of ether in colorless crystals which decomposed above 270°. When picric acid was added to an aqueous solution of this salt a beautiful, crystalline picrate separated. It crystallized from hot water in distorted prisms, which decomposed at 223–224° with effervescence. A mixture of this salt and the picrate of *p*-aminophenylethylamine[1] melted at exactly the same temperature. The salt was dried for analysis (Kjeldahl) at 100–110°.

Calculated for $C_8H_{12}N_2(C_6H_2O_7N_3)_2$: N, 18.91: found: N, 18.9.

Alkylation of Paranitrophenylethylamine with Methyliodide.—Four grams of this amine and 13.5 grams of methyliodide (4 mols.) were dissolved in ether. There was evidence of a reaction at once. Heat was evolved and a salt began to separate in a few minutes. The mixture was heated to boiling for about 18 hours, filtered, and the salt dissolved in cold water. When an excess of alkali was added to this solution a basic oil separated, which was dissolved in ether and dried over potassium hydroxide. It reacted with phenylisothiocyanate, giving a colorless thiourea which crystallized from 95 per cent. alcohol in stout prisms melting at 136–137°. The compound was identified as 1-phenyl-2-paranitrophenylethylthiourea.[1] A mixture of the substance and the above thiourea melted at the same temperature.

Calculated for $C_{15}H_{15}O_2N_3S$: N, 13.9; found: N, 13.65.

After filtering from the salt above, the ether solution was examined for other products of the reaction. On evaporation, not enough material was obtained for examination.

In a second experiment 11 grams of *p*-nitrophenylethylamine and 18.0 grams of methyliodide were dissolved in methyl alcohol and the solution heated at 100° for 2 hours. On opening the tube there was slight pressure and a strong odor of methyliodide. The excess of alcohol and methyliodide were removed by evaporation on the steam bath when an oily mixture of hydriodides was obtained, which solidified on standing. The salts were dissolved in cold water, dilute sodium hydroxide added to liberate the organic bases and the solution then extracted with ether. An oil was removed by this treatment (see below) but a viscous substance

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[1] Johnson and Guest, *Loc. cit.*

also separated which was not dissolved by ether and finally crystallized in yellow prisms. This substance dissolved easily in warm water and alcohol and separated from alcohol, on cooling, in hexagonal prisms melting at 200–201°. It was not decomposed by warm sodium hydroxide solution and gave a strong test for iodine. The properties of the compound and the analytical determination proved that it was the quaternary salt, *viz.*: *trimethyl-p-nitrophenylethylammonium iodide*, $NO_2C_6H_4CH_2CH_2N(CH_3)_3I$.

Calculated for $C_{11}H_{17}O_2N_2I$: I, 37.85; found: I, 37.79.

When the ether extract (above) was allowed to evaporate a base was obtained which reacted immediately with phenylisothiocyanate at ordinary temperature, giving a thiourea melting at 133–4°. It was identified as 1-phenyl-2-paranitrophenylethylthiourea.[1] A mixture of this compound and the above thiourea melted at the same temperature. A mixture of the compound and 1-phenyl-2,2-methyl-*p*-nitrophenylethylthiourea (see above) melted below 110°.

New Haven, Conn.

[Contribution from the Chemical Laboratory of the University of North Carolina.]

THE BROMINATION OF ANTHRANILIC ACID.

By Alvin S. Wheeler and W. M. Oates.

Received March 21, 1910.

The monobromoaminobenzoic acids have been prepared in most cases by the reduction of the bromonitrobenzoic acids in acid solution with tin, zinc or stannous chloride. The 5-bromoanthranilic acid was obtained in two other ways by Alt,[2] *viz.*: (1) by the oxidation of 5-bromo-2-acetotoluide by potassium permanganate and (2) by the bromination of acetoanthranilic acid. The latter reaction was conducted in aqueous and in acetic acid solution, the only product isolated being the monobromoanthranilic acid. We find that in brominating anthranilic acid directly in acetic acid solution at as low a temperature as possible one-third of the product consists of the 3,5-dibromoanthranilic acid. We[3] find it a most excellent method for preparing both acids. Bogert and Hand[4] employed methods similar to those of Alt.

The dibromoaminobenzoic acids have been prepared similarly. In addition Wachendorff[5] heated *o*-nitrotoluene with bromine at 170°. Bogert and Hand[6] prepared 3,5-dibromoanthranilic acid by treating a

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[1] Johnson and Guest, *Loc. cit.*

[2] Alt, *Ber.*, **22**, 1645 (1889).

[3] Wheeler and Oats, This Journal, **31**, 568 (1909).

[4] Bogert and Hand, *Ibid.*, **27**, 1476 (1905).

[5] Wachendorff, *Ann.*, **185**, 281.

[6] Bogert and Hand, This Journal, **25**, 935 (1903).