219° with gas evolution and slight preliminary softening. It gives a strong Beilstein test.

0.1315 g. subst.; 9.6 cc. N, 771 mm., 23.0°.
Calcd. for $C_{16}H_{13}O_4N_2Cl$: N, 8.43%. Found: N, 8.54%.

***m*-Uraminophenyl Benzoate.**—This substance was prepared in essentially the same way as the *o*-isomer. The yield obtained from 29 g. *m*-uraminophenol was 49 g., melting at 178–80°. Recrystallized twice from 95% alcohol, using bone-black, it forms lenticular plates which dissolve in acetone, boiling water, and very readily in boiling 95% alcohol. Rapidly heated to 175°, then slowly, the benzoate softens above 180° and melts slowly at 183–4° (corr.), a higher figure being obtained if the final heating is not slow.

0.1590 g. subst.; 14.8 cc. N, 767 mm., 22.5°.
Calcd. for $C_{14}H_{12}O_3N_2$: N, 10.93%. Found: N, 10.85%.

***m*-Chloroacetyluraminophenyl Benzoate.**—After 30 minutes' heating the reaction mixture was poured into ice-water, precipitating the substance as a gum which rapidly crystallized. 15 g. of the urea yielded 18 g. of crude product. Recrystallized first from hot acetone by the addition of an equal volume of water, then from 95% alcohol, the benzoate separates in rosets of long, flat needles which dissolve more readily in boiling acetic acid than in the other usual solvents. Rapidly heated to 185° and then slowly, it softens slightly and melts at 188–9.5° to a brown liquid, with slight gas evolution.

0.1591 g. subst.; 11.7 cc. N, 746 mm., 22.5°.
Calc. for $C_{16}H_{13}O_4N_2Cl$: N, 8.43%. Found: N, 8.34%.

NEW YORK CITY.

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.]

UNSYMMETRICAL DERIVATIVES OF AROMATIC DIAMINES.

BY WALTER A. JACOBS AND MICHAEL HEIDELBERGER.

Received May 5, 1917.

In the course of our synthetic work it was found necessary to prepare a number of derivatives of *m*-phenylenediamine, *p*-phenylenediamine, and 2,4-tolylenediamine. It was soon found that, although a great many of the simpler unsymmetrical derivatives of these amines had been made, notably by Schiff and Vanni[1] and Schiff and Ostrogovich,[2] previous workers had been unable to isolate all of these substances in a state of purity or else had recorded properties which we were unable to confirm. For example, Schiff and Ostrogovich state that *p*-aminophenylurea is an easily oxidizable substance melting at 129°, whereas all our preparations

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[1] Schiff and Vanni, *Ann.*, **268**, 305 (1892).

[2] Schiff and Ostrogovich, *Ibid.*, **293**, 371 (1896).

of this compound consisted of stable crystals melting at 162–4°. Other cases of similar discrepancies will be found in the experimental part. In a number of instances substances had been prepared but never described, as in the case of *m*-aminophenylglycine, while in other instances, for example *m*-aminooxanilic acid, we were unable to find satisfactory directions for making substances which have frequently been used in both research and technical work. We have attempted, therefore, to supply some of the missing material, much of which we believe to be of general interest owing to the fundamental nature of the substances involved. A number of new derivatives of the diamines are also described.

EXPERIMENTAL.

1. Derivatives of *m*-Phenylenediamine.

***m*-Aminoacetanilide Hydrochloride.**—Wallach and Schulze[1] describe this substance as melting at about 280°, while Schiff and Ostrogovich[2] give 194° as the softening point. By the method described by the former authors 324 g. commercial *m*-phenylenediamine yielded 178 g. of the salt after recrystallizing by bone-blacking in the minimum amount of hot water, adding an equal volume of 1 : 1 hydrochloric acid, and chilling. Recrystallized again from 95% alcohol the hydrochloride forms transparent plates which melt at 248–51° with preliminary softening to a thick, turbid, yellow liquid which darkens and becomes entirely fluid at about 280°. It is readily soluble in cold, dry methyl alcohol, less readily in cold water or absolute alcohol, and is readily diazotized, yielding a scarlet color with R-salt.

0.1613 g. subst.; 0.1246 g. AgCl.

Calc. for $C_8H_{10}ON_2.HCl$: Cl, 19.00%. Found: Cl, 19.11%.

***m*-Aminoacetanilide.**—The above authors did not isolate this substance in the pure state, while C. Mills and Lawson[3] obtained it by reduction of *m*-nitroacetanilide, describing it as melting at 87–9°. The base is readily obtained by suspending the hydrochloride in a *small* volume of water and adding an excess of concentrated sodium hydroxide solution or concentrated aqueous ammonia. It precipitates as an oil which solidifies on rubbing at 0°. The liquid is decanted and the base pressed out on a porous plate, dried *in vacuo*, and recrystallized twice from benzene, when it forms feathery aggregates of flat needles or long, thin plates which melt at 86.5–87.5° (corr.). It is very readily soluble in the cold in water, acetone, and alcohol, less so in chloroform, and difficultly in benzene.

0.1009 g. subst.; 16.4 cc. N, 760 mm., 24.0°.

Calc. for $C_8H_{10}ON_2$: N, 18.67%. Found: N, 18.68%.

***m*-Chloroacetylaminoacetanilide.** — 10 g. *m*-aminoacetanilide hydro-

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[1] Wallach and Schulze, *Ber.*, 15, 3020 (1882).

[2] *Loc. cit.*, p. 382.

[3] C. Mills and Lawson, *J. Chem. Soc.*, 67, 927 (1895).

chloride were chloroacetylated in 50% acetic acid in the presence of sodium acetate, according to the method given in the preceding paper. The chloroacetyl derivative separated as an oil which crystallized almost immediately. The yield was 10.1 g. Recrystallized from 95% alcohol the substance forms radiating masses of delicate needles which melt at 212–4° with slow decomposition and preliminary softening. It dissolves in boiling water, more easily in boiling 95% alcohol, and readily in boiling acetic acid, while it is almost insoluble in hot chloroform. Boiled with dilute sodium hydroxide solution it splits off chlorine ion.

0.1245 g. subst.; 13.2 cc. N, 760 mm., 21.5°.
Calc. for $C_{10}H_{11}O_2N_2Cl$: N, 12.37%. Found: N, 12.29%.

m-**Acetaminophenylurea,** *m*-$CH_3CONHC_6H_4NHCONH_2$.—Schiff and Ostrogovich[1] describe this substance as crystallizing in reddish needles which melt at 225° and dissolve readily in water. 10 g. *m*-aminoacetanilide hydrochloride were dissolved in 120 cc. water and 2.5 cc. acetic acid added. The solution was cooled with ice and treated with a concentrated solution of 4.5 g. potassium cyanate. The urea separated on scratching in a yield of 8 g. Recrystallized from 95% alcohol it forms colorless aggregates of thin plates which are difficultly soluble in cold water, more easily in cold alcohol or acetic acid, and readily in all these on warming. Rapidly heated to 200°, then slowly, the urea melts at 204–5.5° with gas evolution.

Kjeldahl: 0.1534 g. subst.; 34.1 cc. *N*/14 HCl.
Calc. for $C_9H_{11}O_2N_3$: N, 21.76%. Found: N, 22.23%.

m-**Aminophenylurea Hydrochloride.**—According to Schiff and Ostrogovich[2] this salt forms scales melting at 281–2°. 67 g. *m*-acetaminophenylurea were boiled 15 minutes with 5 parts (375 cc.) of 1 : 1 hydrochloric acid (brought to a boil before adding) and rapidly chilled, causing precipitation of the amino salt. This was filtered off and washed with acetone. The yield was 48 g. Recrystallized from 85% alcohol, adding a drop of concentrated hydrochloric acid before cooling, it forms feathery aggregates of microscopic spears which are soluble in cold water but difficultly so in cold alcohol. It sinters and softens at 220–30° and gradually melts and decomposes above 275°.

0.1790 g. subst.; 0.1372 g. AgCl.
Calc. for $C_7H_9ON_3.HCl$: Cl, 18.90%. Found: Cl, 18.96%.

m-**Aminophenylurea.**—The authors quoted above were unable to isolate the free base from their hydrochloride, although this presented no difficulty in the case of our samples of the salt. A portion was suspended in a small volume of water and an excess of concentrated aqueous ammonia added. The base separated from the clear solution on scratching. It

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[1] *Loc. cit.*, p. 383.

[2] *Ibid.*, p. 384.

was filtered off, washed with a little ice-water, and recrystallized from water, forming radiating groups of long, prismatic needles. The urea melts at 128–30° (corr.) with slight, slow gas evolution and slight preliminary softening, and dissolves very much more easily in hot water or alcohol than in the cold. It is almost insoluble in hot benzene or chloroform, but dissolves in acetone. It is readily diazotized, giving a red color with R-salt.

0.0956 g. subst.; 22.8 cc. N, 759 mm., 18.5°.
Calc. for $C_7H_9ON_3$: N, 27.81%. Found: N, 27.89%.

m-**Chloroacetylaminophenylurea,** *m*-$ClCH_2CONHC_6H_4NHCONH_2$.—20 g. *m*-aminophenylurea hydrochloride, chloroacetylated by the dilute acetic acid method,[1] gave 19 g. of the acyl derivative. Recrystallized first from 50%, then from 95% alcohol, it forms delicate, felted needles which are difficultly soluble in the usual hot, neutral solvents with the exception of alcohol. Rapidly heated to 190°, then slowly, it melts at 192–3° with gas evolution. Boiled with dilute sodium hydroxide solution it splits off chlorine ion.

0.1172 g. subst.; 19.0 cc. N, 756 mm., 24.0°.
Calc. for $C_9H_{10}O_2N_3Cl$: N, 18.47%. Found: N, 18.53%.

m-**Aminophenylglycine,** *m*-$H_2NC_6H_4NHCH_2CO_2H$.—This substance is mentioned, but not described, in Ger. pat. 96857.[2] We obtained it in 75% yield by reduction of the *m*-nitro compound by the ferrous sulfate and ammonia method, using the procedure outlined in the first paper of this series. The amino acid is very susceptible to oxidation when dissolved and is therefore difficult to obtain free from color. Recrystallized from water containing a few drops of acetic acid it forms pale brown, wedge-shaped crystals which are difficultly soluble in the usual neutral solvents except hot water. Rapidly heated to 185°, then slowly, it melts at 193–4° with gas evolution. In water it gives a deep brown color with ferric chloride, while in a solution in dilute hydrochloric acid sodium nitrite gives rise to an orange-colored solution which does not couple with R-salt.

Kjeldahl: 0.1345 g. subst.; 15.90 cc. 0.1 *N* HCl.
Calc. for $C_8H_{10}O_2N_2$: N, 16.87%. Found: N, 16.57%.

m-**Aminophenylglycine Methyl Ester Dihydrochloride.**—60 g. of the glycine were suspended in 500 cc. dry methyl alcohol and dry hydrochloric acid gas was passed in until saturated. The glycine dissolved, after which the ester salt separated. The mixture was cooled with ice, filtered, and the hydrochloride washed with dry acetone. The yield was excellent. Recrystallized by dissolving in dry methyl alcohol, adding dry ether until faintly turbid, and seeding, the salt was obtained as rosets

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[1] See preceding paper.

[2] Friedländer, *Fortschr. Teerfarben-Fabrik.*, IV, 924.

of minute spears which dissolve in the cold in methyl and ethyl alcohols. Rapidly heated to 190° and then slowly, it softens and decomposes at 196–7°. The salt is readily diazotized, giving a red color with R-salt, and gives a slowly developing brown color with ferric chloride in aqueous solution. With sodium carbonate solution it gave the ester as an oil which did not solidify at 0°.

0.1879 g. subst.; 0.2161 g. AgCl.
Calc. for $C_9H_{12}O_2N_2.2HCl$: Cl, 28.41%. Found: Cl, 28.46%.

***m*-Aminophenylglycinamide,** *m*-$H_2NC_6H_4NHCH_2CONH_2$.—The methyl ester dihydrochloride obtained from 60 g. *m*-aminophenylglycine was covered, with cooling, with 350 cc. concentrated aqueous ammonia and occasionally shaken. A clear solution was first obtained, from which the amide soon began to separate. After standing overnight, this was filtered off, washed with 10 cc. ice-water, and recrystallized from 95 % alcohol. The yield was 15 g. A further amount was obtained, however, by concentrating the ammoniacal solution. The amide forms rosets of flat needles which soften at 145° and melt at 145.5–6.5° (corr.). It dissolves readily in methyl alcohol, is soluble in cold water, difficultly in cold 95% alcohol, cold acetone, and scarcely in benzene. It is readily diazotized, giving an orange-red color with R-salt.

Kjeldahl: 0.2074 g. subst.; 37.35 cc. 0.1 *N* HCl.
Calc. for $C_8H_{11}ON_3$: N, 25.45%. Found: N, 25.23%.

***m*-Aminooxanilic Acid,** *m*-$H_2NC_6H_4NHCOCO_2H$.—Although this substance has been well known ever since its discovery by Klusemann,[1] as is evidenced by its frequent use by other writers and in chemical patents, we were unable to find recorded a satisfactory method for its preparation. Small amounts may be obtained by the modification of Koller's method given below for the preparation of *p*-aminooxanilic acid, but the yield is poor and the method therefore unsuitable for large-scale work. The following procedure was therefore adopted: 100 g. of technical *m*-phenylenediamine were melted and thoroughly mixed with 240 g. of powdered, crystalline oxalic acid. The mixture was heated 1 hour at 115–20° and 2 hours at 140°, remaining solid during the entire period. After cooling, the product was powdered, suspended in about 4 liters of water and treated with aqueous ammonia until completely dissolved. Calcium chloride was then added in excess, the calcium oxalate filtered off, and acetic acid added to the filtrate until strongly acid. The amino acid quickly separated on scratching. The yield was 85 g. As no complete or accurate description of the substance appears to have been given, the following facts are presented: Recrystallized from water, the acid forms radiating masses of delicate needles which contain one molecule of water of crystallization. The anhydrous acid, rapidly heated to 240°

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[1] Klusemann, *Ber.*, 7, 1263 (1874)

and then slowly, turns yellow and finally melts and decomposes at 245°, not 225°, as given by Schiff and Ostrogovich.[1] It is readily diazotized, giving a deep red color with R-salt.

Air-dry: 0.5428 g. subst.; 0.0468 g. loss. H_2O, 8.62%. Calcd.: 9.09%.
Anhydrous: Kjeldahl: 0.1885 g. subst.; 21.1 cc. 0.1 *N* HCl.
Calc. for $C_8H_8O_3N_2$: N, 15.56%. Found: N, 15.68%.

Attempts were made to convert the acid into the methyl ester by the action of methyl alcohol and hydrochloric acid gas with a view to preparing the amide in this way, but these resulted only in recovery of the acid hydrochloride or, under vigorous treatment, in decomposition. For this reason the amide was made by the steps outlined below.

***m*-Nitrooxanilamide,** *m*-$O_2NC_6H_4NHCOCONH_2$.—17 g. *m*-nitrooxanilic ethyl ester (from 15 g. *m*-nitraniline and 30 g. ethyl oxalate at 160° for 6 hours) were moistened with alcohol and treated with concentrated aqueous ammonia in excess, with vigorous stirring. Formation of the amide began almost immediately, but the mixture was shaken on the machine for 1 hour and then heated on the water bath for 15 minutes. The pasty mass was cooled, filtered, and the substance washed with water and alcohol. The yield of crude amide was 13.8 g. Recrystallized from acetic acid it forms aggregates of minute needles which are more soluble in hot acetic acid than in the other usual solvents. Rapidly heated to 265° and then slowly, it sinters and melts at 268–9° with effervescence.

0.1012 g. subst.; 17.4 cc. N, 760 mm., 21.5°.
Calc. for $C_8H_7O_4N_3$: N, 20.09%. Found: N, 19.94%.

***m*-Aminooxanilamide,** *m*-$H_2NC_6H_4NHCOCONH_2$.—26.2 g. of the nitro amide were ground to a thin paste with hot water and reduced by the ferrous sulfate and ammonia method (see the first paper of this series). The aminoamide separated from the ammoniacal filtrate on cooling, the yield being 17.4 g. Recrystallized from water, with bone-blacking, it forms thin, colorless, hexagonal platelets which melt at 191–1.5° (corr.) with slight preliminary softening. The amide is soluble in acetone, hot water, hot 95% alcohol, difficultly in hot chloroform or absolute alcohol, almost insoluble in hot benzene, and separates from the solution in absolute alcohol in woolly masses of delicate needles. It is readily diazotized, yielding a scarlet precipitate with R-salt.

0.1163 g. subst.; 23.75 cc. N, 760 mm., 22.0°.
Calc. for $C_8H_7O_2N_3$: N, 23.46%. Found: N, 23.60%.

***m*-Chloroacetylaminooxanilamide,** *m*-$ClCH_2CONHC_6H_4NHCOCONH_2$.—10 g. of the aminoamide were dissolved in 250 cc. 50% acetic acid containing 15 g. sodium acetate, cooled in ice-water, and treated with 7.5 g. chloroacetyl chloride in small portions, with shaking and cooling. The

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[1] *Loc. cit.*, p 385.

acyl derivative separated immediately and was filtered off after half an hour's standing and washed with 50% acetic acid and water. The yield was 13 g. A small portion was recrystallized from boiling water, in which it is difficultly soluble, and separated as arborescent masses of minute needles with a faint pinkish tinge. The compound darkens above 270° and decomposes slowly at 281°, the highest temperature reached by the bath. It gives the Beilstein test, and dissolves more easily in boiling acetic acid than in the other usual solvents, in which it is very sparingly soluble.

0.1087 g. subst.; 15.5 cc. N, 765 mm., 20.5°.
Calc. for $C_{10}H_{10}O_3N_3Cl$: N, 16.44%. Found: N, 16.70%.

m-**Uraminooxanilamide,** *m*-$H_2NCONHC_6H_4NHCOCONH_2$.—A solution of 6 g. potassium cyanate was added to a well-chilled solution of 12 g. *m*-aminooxanilamide in 200 cc. 50% acetic acid. The urea separated almost immediately, and was filtered off and washed with water. The yield obtained was 14 g. A small portion was recrystallized from water, with bone-blacking and addition of a few drops of ammonia to the filtered solution. It separates as voluminous, hair-like needles which soften, turn slightly yellow, and decompose somewhat above 260° but do not melt below 280°. The urea is very difficultly soluble in the usual solvents.

Kjeldahl: 0.0645 g. subst.; 11.65 cc. 0.1 *N* HCl.
Calc. for $C_9H_{10}O_3N_4$: N, 25.23%. Found: N, 25.30%.

m-**Chloroacetyluraminooxanilamide,** *m*-$ClCH_2CONHCONHC_6H_4NHCOCONH_2$.—6 cc. chloroacetyl chloride were added to a suspension of 11 g. of finely powdered *m*-uraminooxanilamide in 35 g. of molten chloroacetic acid. The urea dissolved on heating on the water bath, except for a few lumps which had to be broken up with a stirring rod before solution would take place. After half an hour's heating the chloroacetyl derivative started to crystallize, whereupon the mixture was diluted with water. The product was filtered off, ground up in a mortar with water, and treated with sodium acetate solution until neutral to congo red. After filtering, washing, and drying, the substance weighed 11.5 g. Recrystallized from acetic acid, in which it is more soluble than in the other usual solvents, it forms minute plates and rosets of minute, flat needles. Rapidly heated to 230° and then slowly, it decomposes at 233–4° with preliminary darkening and softening. The compound dissolves in boiling, dilute sodium hydroxide solution, splitting off chlorine ion.

Kjeldahl: 0.1428 g. subst.; 19.2 cc. 0.1 *N* HCl.
Calc. for $C_{11}H_{11}O_4N_4Cl$: N, 18.77%. Found: N, 18.83%.

m-**Nitromalonanilic Ethyl Ester,** *m*-$O_2NC_6H_4NHCOCH_2CO_2C_2H_5$.—30 g. *m*-nitraniline and 50 g. malonic ester (1.5 mols.) were heated in an oil bath to 200°, at which point vigorous evolution of alcohol began. The melt was heated one hour at 200–10°, allowing most of the alcohol to boil off through an air-condenser, according to the method used by Chattaway and Mason[1] in obtaining halogen-substituted malonanilic compounds. The excess of malonic ester was then distilled off *in vacuo* and most of the thick, dark residue withdrawn for conversion into the amide. A portion was rubbed with alcohol in a freezing mixture until crystalline and pressed out on a porous plate at 0°. The remaining solid was dissolved in boiling benzene, cooled, filtered from the *m*-nitromalonanilide that separated (see below), and evaporated to dryness. On cooling, the residue crystallized to a mass of long needles. This was dissolved in a little hot benzene and fractionally precipitated by ligroin, discarding the first red, oily fractions and keeping the lighter deposit which subsequently came down and soon crystallized on rubbing. This was recrystallized from ligroin, forming delicate, cream-colored needles which melted at 73.5–4° (corr.) with slight preliminary softening and dissolved readily in the usual solvents except water and ligroin.

0.1387 g. subst.; 13.2 cc. N, 768 mm., 22.5°.
Calc. for $C_{11}H_{12}O_5N_2$: N, 11.11%. Found: N, 11.11%.

***m*-Nitromalonanilide,** *m*-$O_2NC_6H_4NHCOCH_2CONHC_6H_4NO_2$.—Most of the crude, tarry ester obtained above was thinned with an equal volume of alcohol and shaken on the machine with 2 volumes of concentrated aqueous ammonia. The microcrystalline paste was filtered and the residue washed with water and recrystallized from 95% alcohol, part separating crystalline and part as a jelly which gradually solidified when stirred at frequent intervals. The yield of crude product was 25 g. If any *m*-nitromalonanilamide was present it passed into the mother liquors on recrystallization, for, recrystallized twice from acetic acid and once from amyl alcohol the crude product yielded only *m*-nitromalonanilide in the form of cream-colored needles which melted and resolidified at about 173–7° and finally melted at 198–200° (corr.). Owing to the pressure of other work the more soluble fractions were not investigated. The anilide is soluble in acetone, hot acetic acid, hot amyl alcohol, and almost insoluble in boiling water or benzene.

0.1000 g. subst.; 14.2 cc. N, 759 mm., 24.0°.
Calc. for $C_{15}H_{12}O_6N_4$: N, 16.28%. Found: N, 16.30%.

***m*-Aminomalonanilide,** *m*-$H_2NC_6H_4NHCOCH_2CONHC_6H_4NH_2$.—Most of the crude material containing the nitroanilide was reduced by the ferrous sulfate and ammonia method. A small amount of the aminoanilide separated from the ammoniacal filtrate on cooling. This was purified by suspending in water, adding a slight excess of dilute hydrochloric acid to dissolve the base, adding a little bone-black, and filtering. The base was then precipitated by the addition of ammonia and recrystallized from 50% alcohol. It forms glistening, cream-colored needles which melt

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[1] Chattaway and Mason, *J. Chem. Soc.*, 97, 339 (1910).

at 180.5° (corr.) with slight preliminary softening and are soluble in acetone, boiling water or alcohol, and difficultly in hot benzene. It is readily diazotized, yielding a difficultly soluble scarlet dye with R-salt, and gives a brown color with ferric chloride when dissolved in hot water.

0.1053 g. subst.; 18.0 cc. N, 757 mm., 21.5°.
Calcd. for $C_{15}H_{16}O_2N_4$: N, 19.72%. Found: N, 19.73%.

2. Unsymmetrical Derivatives of *p*-Phenylenediamine.

***p*-Chloroacetylaminoacetanilide,** *p*-$ClCH_2CONHC_6H_4NHCOCH_3$.—15 g. *p*-aminoacetanilide were dissolved in a mixture of 75 cc. acetic acid and 75 cc. saturated sodium acetate solution and chloroacetylated as in previous examples. The yield was 21 g. Recrystallized from acetic acid the substance forms minute prisms with wedge-shaped ends, which darken above 260° and decompose at 265–70°. The compound is very difficultly soluble in the usual solvents.

0.1509 g. subst.; 13.50 cc. 0.1 *N* HCl. 0.2500 g. subst.; 0.1557 g. AgCl.
Calc. for $C_{10}H_{11}O_2N_2Cl$: N, 12.37%; Cl, 15.65%. Found: N, 12.53%; Cl, 15.41%.

***p*-Acetaminophenylurea.**—Owing to the difficulty of obtaining potassium cyanate at the present time the following method of preparation of this urea may be of interest: 100 g. *p*-aminoacetanilide were dissolved in 5 parts of 50% acetic acid, cooled to 0°, turbined, and treated slowly with an aqueous suspension of 65 g. of commercial sodium cyanate. The urea separated on standing and was filtered off and washed with water. The yield was 90 g., corresponding in properties to those given by Schiff and Ostrogovich.[1]

***p*-Acetaminophenylchloroacetylurea,** *p*-$CH_3CONHC_6H_4NHCONHCO$-CH_2Cl.—11 g. *p*-acetaminophenylurea were dissolved in 30 g. chloroacetic acid on the water bath, treated with 5.5 cc. chloroacetyl chloride, and heated one-half hour on the water bath. The solution was then poured into water and the precipitate filtered off, thoroughly agitated with hot water containing enough sodium acetate to combine with any free hydrochloric acid present, filtered again and washed with water and alcohol. The yield was 11 g. A small portion was recrystallized for analysis from amyl alcohol, forming lenticular micro-platelets which are very difficultly soluble in the usual neutral solvents. Rapidly heated to 230° and then slowly, it melts and decomposes at 235–7°, with preliminary softening.

0.1278 g. subst.; 17.2 cc. N, 757 mm., 25.0°.
Calc. for $C_{11}H_{12}O_3N_3Cl$: N, 15.59%. Found: N, 15.36%.

***p*-Aminophenylurea Hydrochloride.**—This salt, presumably obtained by Schiff and Ostrogovich, was prepared by us as follows: One liter of boiling 1 : 1 hydrochloric acid was poured onto 200 g. *p*-acetamino-

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[1] *Loc. cit.*, p. 375.

phenylurea and the mixture boiled 15 minutes. On rapid chilling the hydrochloride separated at once. This was filtered off, washed with 10% aqueous hydrochloric acid and purified by dissolving in the minimum amount of hot water, adding concentrated hydrochloric acid until the concentration of acid reached about 10%, and chilling rapidly. 100 g. of the salt separated as micaceous plates which did not melt below 280°. Its aqueous solution gives a deep purple color with ferric chloride and is readily diazotized, yielding a purplish red dye with R-salt.

0.1579 g. subst.; 31.0 cc. N, 762 mm., 23.5°.
Calc. for $C_7H_9ON_3.HCl$: N, 22.40%. Found: N, 22.65%.

***p*-Aminophenylurea.**—When the above hydrochloride is dissolved in a small amount of warm water and treated with an excess of sodium hydroxide or ammonia the free base separates on rubbing as glistening platelets. Schiff and Ostrogovich[1] were unable to isolate the urea in this simple way from their sample of the hydrochloride, and their description of the urea itself is such as to throw doubt on their having had the compound in their hands, although Pierron,[2] who claims to have prepared the substance both by reduction of the nitrourea and by hydrolysis of the cyanamide, gives the same melting point as Schiff and Ostrogovich found, namely, 129°. We found that the base, when recrystallized from a small volume of water, with bone-blacking, forms flat, colorless, glistening needles or long platelets which contain water of crystallization which is only slowly lost on exposure to the air. In one case the compound came to constant weight in the air while still containing one-half molecule of water of crystallization. The urea melts with slight preliminary softening at 162–4° with gas evolution and resolidification, the decomposition product remaining solid below 285°. It is not readily oxidized in the air, as claimed by Schiff and Ostrogovich, and is readily diazotized, coupling with R-salt to yield a purplish red dye. In aqueous solution it gives a brown color with a drop of ferric chloride solution, and deposits purple flocks on addition of a larger amount of the reagent. The urea is soluble in water or acetone, sparingly in cold absolute alcohol, readily in hot, and is almost insoluble in benzene or ether.

Kjeldahl: 0.0963 g. subst.; 26.95 cc. *N*/14 HCl.
Calc. for $C_7H_9ON_3$: N, 27.81%. Found: N, 27.98%.

***p*-Chloroacetylaminophenylurea,** *p*-$ClCH_2CONHC_6H_4NHCONH_2$.—38 g. *p*-aminophenylurea hydrochloride were dissolved by warming in a mixture of 150 cc. acetic acid and 150 cc. saturated sodium acetate solution and were then chloroacetylated as in previous examples. After recrystallization from 50% alcohol the yield was 32 g. Recrystallized again from the same solvent, using bone-black, the acyl derivative forms colorless

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[1] *Loc. cit.*, p. 376.

[2] Pierron, *Ann. chim. phys.*, [8] 15, 181, 188 (1908).

hairs and aggregates of flat needles which are difficultly soluble in the usual neutral solvents. When rapidly heated, the substance melts completely at about 225° with gas evolution and resolidification to a mass which does not melt below 285°, while if the heating is slower, it melts partly at 212–3° with gas evolution and resolidification.

Kjeldahl: 0.1315 g. subst.. 17.20 cc. 0.1 *N* HCl.
Calc. for $C_9H_{10}O_2N_3Cl$: N, 18.47%. Found: N, 18.32%.

The glycine derivatives described below were encountered in attempts to obtain good yields of *p*-aminophenylglycine by a convenient method. That involving the reduction of *p*-nitrophenylglycine proved unsuitable because of the poor yields of the nitro compound obtained when the directions given in Ger. pat. 88433[1] were followed. The preparation of the acetyl derivative was then attempted by reacting *p*-aminoacetanilide with chloroacetic acid in aqueous solution, and while this yielded fairly satisfactory results for further synthetic work, the product contained considerable quantities of the diglycine described in the next paragraph, which was the only substance isolated analytically pure, as the soluble *p*-acetaminophenylglycine passed into the mother liquors on recrystallization. Excellent results were finally obtained as described below by the interaction of *p*-aminoacetanilide with chloroacetic ester in alcoholic solution.

***p*-Acetaminophenyldiglycine,** *p*-$CH_3CONHC_6H_4N(CH_2CO_2H)_2$.—10 g. *p*-aminoacetanilide were suspended in 50 cc. water and boiled until neutral with one molecular equivalent each of chloroacetic acid and sodium hydroxide. Half the amounts of chloroacetic acid and alkali were again added and the mixture boiled until neutral once more. After cooling and filtering, the acetamino acid was precipitated by acidifying the solution with hydrochloric acid until acid to congo red. The crude acid was decolorized by boiling with 85% alcohol containing acetic acid and was then recrystallized from a large volume of water, forming sheaves of almost colorless needles which dissolve in boiling acetic acid with gas evolution. Rapidly heated to 230° and then slowly, the acid darkens slightly above 210° and melts with effervescence at 234–5°.

0.1328 g. subst.; 12.45 cc. N, 763 mm., 22.5°.
Calc. for $C_{12}H_{14}O_5N_2$: N, 10.55%. Found: N, 10.87%.

p-Aminophenylglycine was finally prepared as follows:

***p*-Acetaminophenylglycine Ethyl Ester,** *p*-$CH_3CONHC_6H_4NHCH_2CO_2C_2H_5$.—175 g. *p*-aminoacetanilide were dissolved in 750 cc. hot 50% alcohol and boiled 1.5 hours under a reflux condenser with 76 g. ethyl chloroacetate. On cooling in the ice box the solution set to a solid mass. This was disintegrated, filtered off, and washed thoroughly with water in order

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[1] Friedländer, *Festschr. Teerfarben-Fabrik.*, IV, 1156.

to remove the difficultly soluble aminoacetanilide hydrochloride. The yield of crude ester was 100 g. Most of the unused aminoacetanilide can be recovered from the filtrate by neutralization and saturation with salt. Recrystallized first from 95% alcohol, then from benzene, the ester forms rosets of long, delicate needles which melt at 124–5° (corr.) with slight preliminary softening. It is readily soluble in acetone, chloroform, hot benzene, alcohol, or water, and less readily so in the last three in the cold.

Kjeldahl: 0.1336 g. subst.; 11.25 cc. 0.1 *N* HCl.
Calc. for $C_{12}H_{16}O_3N_2$: N, 11.87%. Found: N, 11.80%.

***p*-Aminophenylglycine.**—104 g. crude *p*-acetaminophenylglycine ethyl ester were boiled one hour under a reflux condenser with 520 cc. 1 : 1 hydrochloric acid. The solution was cooled and the precipitate of amino acid hydrochloride filtered off, washed with a little 1 : 1 hydrochloric acid, dissolved in water, and neutralized to congo red with saturated sodium acetate solution. The precipitate of aminophenylglycine was filtered off and washed with water. The yield was 61 g. Recrystallized from water containing a few drops of acetic acid, using bone-black, the glycine was obtained as almost colorless, glistening leaflets which contain one molecule of water of crystallization. On boiling these with absolute alcohol, the crystalline form suddenly changes to microscopic hairs, probably due to dehydration of the hydrate. Air-dry, or anhydrous, when rapidly heated to 220° and then slowly, the compound melts and decomposes at 222–3° with preliminary slight decomposition, not at 208°, as given in Ger. pat. 88433,[1] according to which the aminoglycine is obtained by reduction of the nitroglycine with tin and hydrochloric acid.

0.6162 g. subst.; 0.0611 g. loss. Calc.: 1 H_2O, 9.79%. Found: 9.91%.
0.1145 g. subst.; 16.6 cc. N, 752 mm., 19.5°.
Calc. for $C_8H_{10}O_2N_2$: N, 16.87%. Found: N, 16.74%.

***p*-Aminophenylglycine Ethyl Ester Dihydrochloride.**—7.5 g. of recrystallized *p*-acetaminophenylglycine ethyl ester were dissolved in 40 cc. absolute alcohol which had been saturated at room temperature with dry hydrochloric acid gas. The solution was boiled under a reflux condenser for three-quarters of an hour. The crystalline product was filtered off on cooling and washed with a little absolute alcohol. The yield of dihydrochloride was 7.5 g., melting at 201–2° with gas evolution and preliminary softening. The salt is readily soluble in the cold in water or dry methyl alcohol, but rather difficultly in absolute alcohol. In dilute hydrochloric acid it gives a deep, olive-green color with sodium nitrite. A concentrated aqueous solution, treated with sodium carbonate, deposits the ester as an oil.

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[1] *Loc. cit.*

0.1296 g. subst.; 12.1 cc. N, 764 mm., 22.5°. Carius: 0.1605 g. subst.; 0.1703 g. AgCl.

Calc. for $C_{10}H_{14}O_2N_2.2HCl$: N, 10.48%; Cl, 26.55%. Found: N, 10.85%; Cl, 26.25%.

***p*-Aminophenylglycinamide.**—108 g. of the ethyl ester dihydrochloride were carefully treated, with chilling, with 3 parts of concentrated aqueous ammonia. The mixture, which darkened and soon began to deposit the amide, was allowed to stand in the cold for 2 days, after which the amide was filtered off, washed with a little alcohol, and recrystallized from 95% alcohol. The yield was 30 g. Again recrystallized from the same solvent, using bone-black, it forms crusts consisting of slightly brownish aggregates of thin plates which melt to a brown liquid at 161–4° with slight preliminary softening. It is soluble in cold water or 95% alcohol, very much more so on heating, and dissolves more readily in acetone than in benzene. In aqueous solution it gives an olive color with ferric chloride, changing to purple. The amide is readily diazotized, the solution giving a red color with R-salt.

0.1036 g. subst.; 23.2 cc. N, 753 mm., 27.0°.
Calc. for $C_8H_{11}ON_3$: N, 25.45%. Found: 25.25%.

***p*-Aminooxanilic Acid,** *p*-$H_2NC_6H_4NHCOCO_2H$.—This substance was prepared essentially as described by Koller,[1] except that, in order to avoid precipitation of the oxalate of the acid instead of the acid itself, as sometimes happened, it was found advisable to take up the entire reaction mixture in a large volume of water, add aqueous sodium hydroxide solution until alkaline, and precipitate the unchanged oxalic acid with calcium chloride solution. The aminooxanilic acid then separates from the filtrate on adding concentrated hydrochloric acid until the reaction is just faintly blue to congo red paper. The resulting product may be used for further synthetic work without recrystallization.

***p*-Chloroacetylaminooxanilic Acid,** *p*-$ClCH_2CONHC_6H_4NHCOCO_2H$.—Owing to the fact that *p*-aminooxanilic acid is practically insoluble in cold 50% acetic acid it was chloroacetylated by the method usually employed by us for the chloroacetylation of ureas (see preceding paper). 10 g. *p*-aminooxanilic acid were suspended in molten chloroacetic acid and treated with 5 cc. chloroacetyl chloride. Interaction occurred at once, with liberation of hydrochloric acid. After 15 minutes on the water bath the mixture was diluted with water, treated with an excess of hydrochloric acid, and the acyl derivative filtered off and washed with acetone. The yield was 13 g. The substance is extremely difficultly soluble in the usual solvents and forms a sparingly soluble sodium salt when an attempt is made to dissolve it in sodium hydroxide solution. A small portion was therefore purified by suspending in hot water, adding an insufficient

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[1] Koller, *Ber.*, 36, 413 (1903).

amount of ammonia, filtering, and adding hydrochloric acid to the cooled filtrate. The acid precipitated as a gelatinous mass which soon changed to radiating masses of microscopic needles and hairs. Rapidly heated to 230°, then slowly, it darkens slightly above 220° and effervesces at about 235°. It gives a strong Beilstein test and becomes strongly triboelectric when rubbed.

Kjeldahl: 0.1748 g. subst.; 19.3 cc. *N*/14 HCl.
Calc. for $C_{10}H_9O_4N_2Cl$: N, 10.92%. Found: N, 11.04%.

***p*-Aminooxanilic Methyl Ester Hydrochloride.**—19.4 g. *p*-aminooxanilic acid were suspended in 200 cc. dry methyl alcohol and turbined, passing in a vigorous stream of dry hydrochloric acid gas through a wide tube to avoid the clogging which otherwise occurs. After a short time the amino acid went into solution, and the ester hydrochloride then separated. This was filtered off, washed with a little dry methyl alcohol, and dried *in vacuo* over calcium chloride and potassium hydroxide. The yield was 22.4 g. Recrystallized from 85% alcohol it forms aggregates of long, thin, slightly purplish plates, which, when rapidly heated, turn yellow above 220° but do not melt below 280°. The salt is soluble in water, and difficultly soluble in hot absolute alcohol or cold, dry methyl alcohol.

0.1417 g. subst.; 0.0858 g. AgCl.
Calc. for $C_9H_{10}O_3N_2.HCl$: Cl, 15.38%. Found: Cl, 14.98%.

***p*-Aminooxanilic Methyl Ester.**—A supersaturated solution of the hydrochloride was obtained by rapidly cooling a hot, concentrated solution. To this was added a slight excess of 10% sodium carbonate solution, precipitating the ester. This was filtered off, washed with a little cold water, and recrystallized from water, bone-blacking the hot solution. It forms greenish yellow, silky needles which soften at 128° and melt at 129–30° (corr.), resolidifying on cooling. The melting point is unchanged by another recrystallization from benzene. The ester is difficultly soluble in cold benzene, somewhat soluble in cold water, and more readily so in cold 95% alcohol or chloroform. An aqueous suspension gives a slowly-developing reddish brown color with ferric chloride. The ester is also readily diazotized, giving a red dye with R-salt.

Kjeldahl: 0.1423 cc. subst.; 14.45 cc. 0.1 *N* HCl.
Calc. for $C_9H_{10}O_3N_2$: N, 14.44%. Found: N, 14.23%.

***p*-Aminooxanilamide,** *p*-$H_2NC_6H_4NHCOCONH_2$.—22 g. powdered *p*-aminooxanilic methyl ester hydrochloride were added in small amounts to a cold, well-stirred, concentrated ammonia solution containing a little alcohol. A few lumps were pressed out with a stirring rod and the pasty mixture was allowed to stand overnight protected from the air. The product was filtered off, washed with a little water, and recrystallized from boiling water, from which it separates as slightly purplish microcrystals which melt at 217–8° to a dark tar. The yield was 10 g. The amide is somewhat soluble in cold water, readily in hot, and dissolves also in acetone, hot 95% alcohol, and boiling ethyl acetate. The aqueous solution gives a slowly-developing purplish color with ferric chloride and, on diazotization and coupling with R-salt, yields a purplish red dye.

Kjeldahl: 0.1537 g. subst.; 25.8 cc. 0.1 *N* HCl.
Calc. for $C_8H_9O_2N_3$: N, 23.46%. Found: N, 23.52%.

***p*-Aminooxanilamide** was also prepared by the following series of reactions: Oxanilic ethyl ester was dissolved in concentrated sulfuric acid and treated with a solution of 1 mol. of concentrated nitric acid in concentrated sulfuric acid, keeping the temperature below 20°. After standing for a short time the mixture was poured into ice-water, the *p*-nitrooxanilic ethyl ester crystallizing almost immediately. This was recrystallized from alcohol and then converted into the amide by grinding to a paste with alcohol and adding concentrated aqueous ammonia. After half an hour the product was filtered off and washed with water. A small portion, recrystallized from 95% alcohol gave a good analysis (N, 19.97%; calcd., N, 20.09%) and agreed in all its properties with those described for *p*-nitrooxanilamide by Schultz, Rohde and Herzog.[1] The crude nitroamide, reduced by the ferrous sulfate and ammonia method, yielded the aminoamide, which separated from the ammoniacal filtrate on cooling. A further small quantity could be obtained by again boiling the precipitate of ferric hydroxide with water containing a little ammonia. The amide prepared in this manner was identical in every way with that obtained through the ester, but the yield was not so good, nor was the method as convenient.

***p*-Chloroacetylaminooxanilamide,** *p*-$ClCH_2CONHC_6H_4NHCOCONH_2$.—10 g. of the aminoamide were dissolved in 300 cc. 50% acetic acid containing 15 g. sodium acetate and chloroacetylated as in previous examples. The crude product was purified by warming on the water bath with 50% alcohol and filtering hot. The residue weighed 11 g. A small portion was recrystallized from acetic acid, forming sheaves of microcrystals which did not melt below 280° and were difficultly soluble in the usual solvents.

0.1022 g. subst.; 14.5 cc. N, 751 mm., 21.0°.
Calc. for $C_{10}H_{10}O_3N_3Cl$: N, 16.44%. Found: N, 16.28%.

***p*-Nitromalonanilide,** *p*-$O_2NC_6H_4NHCOCH_2CONHC_6H_4NO_2$.—27.6 g. *p*-nitraniline and 50 g. malonic ester (1.5 mols.) were heated 1 hour at 200–10°, letting the temperature rise to 230° at the end for a few minutes. The excess of malonic ester was distilled off *in vacuo* and the hot residue mixed with about 2 volumes of hot alcohol. The solution was allowed to stand, with occasional rubbing, the anilide gradually crystallizing.

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[1] Schultz, Rohde and Herzog, *J. prakt. Chem.*, [2] 74, 82 (1906).

This was filtered off, washed with a little alcohol (yield 10 g.), and recrystallized twice from 95% alcohol, forming flat, brownish yellow needles which melted at 241–2° with gas evolution and slight preliminary softening. The compound is somewhat soluble in cold acetone, readily in hot, and dissolves also in hot acetic acid or alcohol.

0.1136 g. subst.; 15.95 cc. N, 764 mm., 20.0°.
Calc. for $C_{15}H_{12}O_6N_4$: N, 16.28%. Found: N, 16.45%.

***p*-Nitromalonanilic Ethyl Ester,** p-$O_2NC_6H_4NHCOCH_2CO_2C_2H_5$.—The filtrate from the crude nitromalonanilide was cautiously diluted with water, depositing an oil which gradually crystallized. This was filtered off and dried. The yield was 25 g. Recrystallized from ligroin, in which it is very difficultly soluble, the ester forms pale yellow, hair-like needles or thin, narrow platelets. These melt at 92–5° and are very readily soluble in alcohol or ether, less easily in benzene.

0.1531 g. subst.; 15.4 cc. N, 756 mm., 22.0°.
Calc. for $C_{11}H_{12}O_5N_2$: N, 11.11%. Found: N, 11.58%.

***p*-Nitromalonanilamide,** p-$O_2NC_6H_4NHCOCH_2CONH_2$.—22 g. of the crude ester were dissolved in warm 95% alcohol, filtered, and treated with an equal volume of concentrated aqueous ammonia. The amide separated on standing, after which the mixture was cooled to 0°, filtered, and washed with cold 50% alcohol. The yield of crude product was 14.6 g. Recrystallized from water, adding a few drops of ammonia to the hot, filtered solution, it forms yellow, rhombic platelets which are readily soluble in hot acetic acid, less easily in hot alcohol, water, or acetone, and difficultly in all in the cold. When rapidly heated to 215°, then slowly, it melts at 218–20° with gas evolution.

0.1262 g. subst.; 20.8 cc. N, 755 mm., 23.0°.
Calc. for $C_9H_9O_4N_3$: N, 18.83%. Found: N, 18.89%.

***p*-Aminomalonanilamide,** p-$H_2NC_6H_4NHCOCH_2CONH_2$.—13.5 g. of the crude nitro compound were mixed to a thin paste with hot water and reduced by the ferrous sulfate and ammonia method as in previous examples. The filtrate from the reduction was acidified with acetic acid, concentrated *in vacuo* and the product filtered off. The yield was 9.7 g. Recrystallized first from water, then from 50% alcohol, using boneblack, the amide forms practically colorless, radiating masses of microplatelets which apparently contain one molecule of water of crystallization which is not driven off at 100° *in vacuo*. When rapidly heated it sinters, then melts partly at 200–10° to a purple mass which does not melt entirely below 280°. It is readily diazotized, yielding a deep red, difficultly soluble dye with R-salt, and, in aqueous suspension, gives a slowly developing wine-red color with ferric chloride.

0.1060 g. subst.; 18.35 cc. N, 756 mm., 23.5°.
Calc. for $C_9H_{11}O_3N_3.H_2O$: N, 19.88%. Found: N, 19.83%.

***p*-Chloroacetylaminomalonanilamide.**—5 g. of the once-recrystallized amide were chloroacetylated as in previous examples. The yield of acyl derivative was 6.5 g. Recrystallized from water, with bone-blacking, it forms sheaves of delicate hairs which are difficultly soluble in the usual solvents. Rapidly heated to 240° and then slowly, it melts with decomposition at 243–4°. It gives a strong Beilstein test.

0.1407 g. subst.; 18.8 cc. N, 760 mm., 23.5°.

Calc. for $C_{11}H_{12}O_3N_3Cl$: N, 15.59%. Found: N, 15.38%.

3. Derivatives of 2,4-Tolylenediamine.

2-Amino-4-acetaminotoluene Hydrochloride.—Although this substance was prepared both by Wallach and Schulze[1] and Schiff and Ostrogovich[2] we were unable to find a complete description of it in the literature. The salt was prepared and purified as in the case of *m*-aminoacetanilide hydrochloride (see p. 1448). Starting with 324 g. of commercial 2,4-toluylenediamine, 120 g. of the hydrochloride were obtained. Recrystallized from 95% alcohol it forms delicate needles which, when rapidly heated to 260° and then slowly, decompose at 263–4° with slight preliminary sintering.

0.1829 g. subst.; 0.1314 g. AgCl.

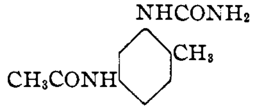
Calc. for $C_9H_{12}ON_2.HCl$: Cl, 17.68%. Found: Cl, 17.78%.

Addition of sodium carbonate to a solution of the salt gives the base, which crystallizes from water in long, brilliant needles which melt at 161–2°, as described in the literature.

2-Chloroacetylamino-4-acetaminotoluene.—10 g. of the above hydrochloride were dissolved in a mixture of 50 cc. acetic acid and 50 cc. saturated sodium acetate solution and chloroacetylated in the usual way. The yield of acyl derivative was 10 g. Recrystallized from 95% alcohol, it forms delicate, felted hairs which are more difficultly soluble in boiling water than in boiling alcohol and are practically insoluble in boiling benzene. Rapidly heated to 225°, then slowly, the substance softens slightly and then melts at 230–1° with slow gas evolution and reddening.

Kjeldahl: 0.1128 g. subst.; 9.4 cc. 0.1 *N* HCl.

Calc. for $C_{11}H_{13}O_2N_2Cl$: N, 11.65%. Found: N, 11.68%.

2-Methyl-5-acetaminophenylurea, 

. — 70 g. aminoacetaminotoluene hydrochloride were dissolved in 800 cc. of warm 50% acetic acid, treated with 35 g. sodium acetate, shaken until a clear solution was obtained, and then cooled to 0°. A solution of 45 g. sodium cyanate was then slowly added, with stirring and chilling. The urea separated almost immediately in practically quantitative yield.

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[1] *Loc. cit.*

[2] *Ibid.*, p. 371.

Recrystallized from water, it forms delicate, felted needles which melt with effervescence at about 240°, resolidifying and then not melting below 280°. The urea dissolves in hot water or alcohol but is almost insoluble in acetone, benzene, or chloroform.

0.1062 g. subst.; 18.5 cc. N, 762 mm., 21.0°.
Calc. for $C_{10}H_{13}O_2N_3$: N, 20.28%. Found: N, 20.29%.

2-Methyl-5-aminophenylurea Hydrochloride.—325 g. of boiling 1 : 1 hydrochloric acid were added to 62.5 g. 2-methyl-5-acetaminophenylurea, after which the solution was boiled 15 minutes and rapidly chilled. The precipitate was filtered off and recrystallized by dissolving in the minimum amount of hot water, cooling, and adding an equal volume of concentrated hydrochloric acid. The resulting salt was washed with 1 : 1 hydrochloric acid and dried. The yield was 30 g. A portion was recrystallized by dissolving in hot 85% alcohol and adding a drop of concentrated hydrochloric acid to the solution before cooling. It forms sheaves of minute needles which soften but do not melt below 280°. The salt is soluble in water or methyl alcohol and difficultly so in hot absolute alcohol. The aqueous solution gives a slowly developing reddish color with ferric chloride.

0.1758 g. subst.; 0.1255 g. AgCl.
Calc. for $C_8H_{11}ON_3.HCl$: Cl, 17.59%. Found: Cl, 17.66%.

2-Methyl-5-aminophenylurea.—A portion of the hydrochloride was dissolved in warm water, cooled, and an excess of ammonia added. The base separated almost immediately as glistening scales. These were filtered off, washed with water, and recrystallized from water, forming star-shaped aggregates of spears. Rapidly heated to 195°, then slowly, the urea melts and effervesces at 199–200°, soon resolidifying and then not melting below 280°. It is difficultly soluble in cold water or 95% alcohol, hot chloroform or acetone, and readily in the first two solvents on boiling. The substance is easily diazotized, giving a dark red color with R-salt. The urea is mentioned by Strauss[1] as having been obtained by Märker, but we were unable to find a description recorded.

0.0903 g. subst.; 19.8 cc. N, 758 mm., 21.5°.
Calc. for $C_8H_{11}ON_3$: N, 25.44%. Found: N, 25.36%.

2-Methyl-5-chloroacetylaminophenylurea.—This substance was prepared as in the case of the chloroacetylaminoacetaminotoluene (see p. 1463). 5 g. of the aminotolylurea hydrochloride yielded 4.6 g. of the acyl derivative. Recrystallized from 95% alcohol, it forms radiating masses of delicate needles which dissolve more readily in hot acetic acid than in the other usual solvents. Rapidly heated to 220° and then slowly, it melts at 224–5° with gas evolution to a liquid which gradually turns

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[1] Strauss, *Ann.*, 148, 159 (1868).

yellow. The aqueous solution, boiled with sodium hydroxide, splits off chlorine ion.

0.1080 g. subst.; 16.0 cc. N, 770 mm., 20.5°.
Calc. for $C_{10}H_{12}O_2N_3Cl$: N, 17.39%. Found: N, 17.46%.

NEW YORK CITY.

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.]

THE PREPARATION OF β-CHLORO- AND β-BROMOPROPIONIC ACIDS.

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Received May 5, 1917.

Of the chief methods to be found in the literature for the preparation of β-chloro- and β-bromopropionic acids only that involving the oxidation by nitric acid of β-chloro- and β-bromopropionaldehydes,[1] obtained by saturation of acrolein with halogen acids, seemed to offer promise for the preparation of considerable quantities of material. Although the yields claimed for this method are excellent, the necessity of working with unpleasant substances led us to seek for a more convenient procedure.

Beckurts and Otto[2] prepared the two acids in question by treating hydracrylic acid with hydrochloric and hydrobromic acids. Hydracrylic acid, in its turn, was obtained by Moureau[3] by hydrolysis of ethylene cyanohydrin, which he prepared easily and satisfactorily by the interaction of ethylene chlorohydrin and potassium cyanide. It occurred to the writers that, starting with ethylene cyanohydrin, the two steps of saponification of the nitrile to the acid and replacement of the hydroxyl group by halogen could be accomplished simultaneously by heating the cyanohydrin with concentrated halogen acid. These expectations were confirmed. Since all of the steps involved may be rapidly and conveniently executed the authors feel that this procedure will prove to be the most satisfactory method for those who have occasion to prepare these substances.

Experimental.

Ethylene Cyanohydrin, HOC_2H_4CN.—The only variation from Moureau's method was that the product was purified by distillation *in vacuo*. 32 g. ethylene chlorohydrin were dissolved in 160 cc. absolute alcohol and boiled under a reflux condenser. To the boiling solution were added, drop by drop, 27.2 g. potassium cyanide dissolved in 42 cc. water. The boiling was continued for eight to ten hours. At the end the

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[1] Krestovnikov, *J. Russ. Phys. Chem. Soc.*, 11, 248 (1879); Lederer, *J. prakt. Chem.*, [2] **42**, 384 (1890).

[2] Beckurts and Otto, *Ber.*, **18**, 226 (1885).

[3] Moureau, *Bull. soc. chim.*, [3] **9**, 426 (1893).