benzoic acids have been compared with their experimental ionization constants and found to agree fairly accurately in all but four cases. For those acids whose ionization constants have been measured by two or more investigators, the agreement between the calculated and experimental values is within the limit of the experimental error in all but one acid.

(4) A method for the determination of the structure of polysubstituted benzoic acids from their ionization has been developed.

(5) Ionization will not distinguish the difference in structure of 2,3- and 2,5-disubstituted benzoic acids where the substituents in 3 and 5 are the same and the substituent in 2 is also the same in both acids.

(6) The equivalency of the positions 3 and 5 with respect to position 1 in the benzene ring has been proven in terms of the free energy of ionization.

(7) The assumption that the free energy of ionization is made up additively of the separate influence of each atom in the molecule of an acid has received further substantiation.

URBANA, ILL.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF MICHIGAN.]

THE FORMATION OF PYRIMIDINES BY USE OF NITROMALONIC ALDEHYDE.[1]

BY WILLIAM J. HALE AND HARVEY C. BRILL.

Received November 7, 1911.

When either acetone or one of its mono- or symmetrical di-substitution products is allowed to act upon nitromalonic aldehyde, a condensation readily takes place. The course of these condensations was thoroughly investigated by Hill and his coworkers.[2] In all of the cases studied, the acetone nucleus was involved with the two aldehyde groups conjointly, and resulted in the formation of six-membered ring compounds—derivatives of benzene. Derivatives of acetone higher than the symmetrical di-substitution products could not be made to enter into the reaction. There arose, therefore, the necessity of explaining these results through the formation of an intermediate product—a derivative of dihydrobenzene. This latter, by the elimination of water, readily underwent a transformation to the benzene type. Two free hydrogen atoms upon either end of the acetone nucleus are thus shown to be a prerequisite for this condensation with nitromalonic aldehyde.

Substances possessing amino groups, and thereby two free hydrogen

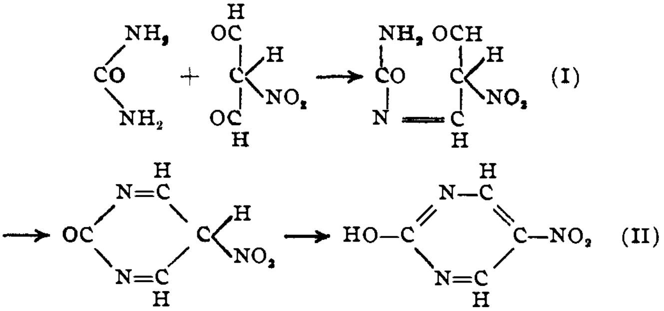
[1] The work described in this article formed part of a thesis presented to the Faculty of the Department of Literature, Science and the Arts of the University of Michigan for the degree of Doctor of Philosophy, by Harvey C. Brill.

[2] *Am. Chem. J.*, 22, 89 (1899); 24, 1 (1900); 33, 1 (1905).

atoms attached to a nitrogen atom, were found very reactive toward nitromalonic aldehyde, but beyond the monoamino derivatives Hill and his coworkers did not proceed.

From the facts thus stated and from the ideas so freely presented to one of us by Professor Hill himself, we determined to investigate this action of nitromalonic aldehyde upon the α-diamino compounds. If analogy might hold, then, urea, the simplest member of that class of α-diamino compounds possessing a carbonyl group in the same relative position as in acetone, should condense with this aldehyde to give a six-membered ring containing two nitrogen atoms in the meta position—namely, a pyrimidine. Pinner[1] has accomplished the synthesis of pyrimidines by making use of various amidines with β-diketones or ketonic esters; in all cases the reactions ran quite smoothly and with good yields.

The reaction of nitromalonic aldehyde with urea is best accomplished in aqueous solution. Sodium hydroxide was used as a condensing agent just as in the work upon acetone derivatives already cited. The results, however, were often bettered by use of piperidine in this same capacity. The solutions soon acquired a yellow color and later developed a deep red. Upon acidification a semi-crystallin, faintly yellow precipitate appeared in fair quantity, and later, upon standing, the mother liquors yielded a yellow leaf-like precipitate in much smaller quantity. The first product (I) melted at 154° (cor.) and proved to be a monoureide of nitromalonic aldehyde. The second product (II) melting at 203.5° (cor.) was shown to be the pyrimidine anticipated. We may represent the reaction as follows:



The monoureide is a much less stable compound than the pyrimidine. It contains, as the formula indicates, a free aldehyde group readily recognizable by characteristic reactions. The monoxime (III) may easily be prepared, but the monanil (IV) offered considerable difficulty. The action of aniline upon the monoureide had a tendency to replace the urea nucleus itself and form at once the monanil of nitromalonic aldehyde[2]

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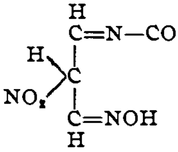
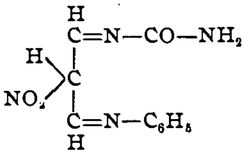
[1] *Ber.*, 23, 161 (1890); 26, 2125 (1893).

[2] *Am. Chem. J.*, 22, 99 (1899).

together with free urea. In order to effect this combination it was necessary first to prepare the nitromalonic aldehyde monanil and suspend this in alcohol containing the theoretical amount of urea (1 mol.). Into this solution was passed a current of dry hydrogen chloride. After standing, the long slender red needles of nitromalonic monoureide anil made their appearance. Similar attempts to prepare a phenylhydrazone of this monoureide were unsuccessful. Phenylhydrazine replaces the urea nucleus and leads at once to the 1-phenyl-4-nitropyrazole.[1] Several salts of the monoureide were made and analyzed.

(III)

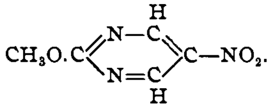




(IV)

It is evident that the monoureide is only an intermediate step in the formation of a dihydropyrimidine, and that this immediately passes over into a pyrimidine by the loss of one molecule of water. This transformation runs poorly at best, but is favored by the presence of a dehydrating agent such as is the excess of sulfuric acid added to the original reaction-mixture. Hydrochloric acid is not as effective. The slight solubility of this monoureide in the acidified mother liquor offers only small chance for any appreciable formation of pyrimidine. The yield of pyrimidine, however, may be substantially increased by warming the original reaction-mixture to about 40° before acidification. Again, the monoureide when dissolved in acetic anhydride and warmed either alone, or with the presence of sulfuric acid, or anhydrous hydrogen chloride, underwent a partial transformation into the pyrimidine. Attempts carried out under pressure were altogether disastrous. The most effective method for bringing about this further condensation consisted in the use of sodium ethylate upon the warm alcoholic solution of the monoureide. Acidification of the final mixture gave a fair yield of pyrimidine. The methyl ether of this pyrimidine was prepared and shown to have a constitution corresponding to a 5-nitro-2-methoxypyrimidine (V):

(V)



The probable formation of a dihydropyrimidine as the intermediate product in passing from the monoureide to the pyrimidine has a possible substantiation in the work of P. N. Evans[2] and A. and C. Combes.[3]

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[1] *Am. Chem. J.*, 22, 105 (1899).

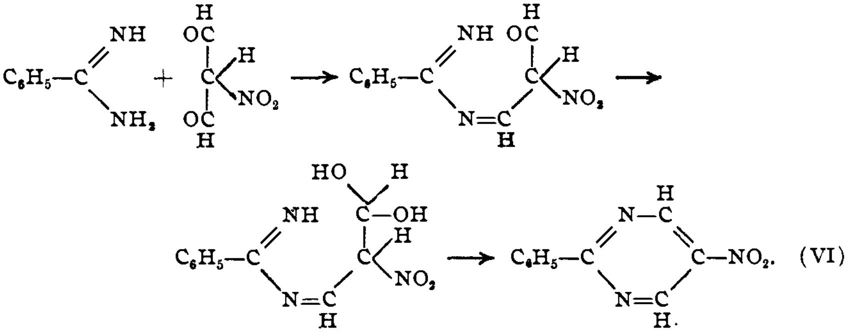
[2] *J. prakt. Chem.*, [2] 48, 489 (1893).

[3] *Bull. soc. chim., Paris*, [3] 7, 788 (1892).

These investigators assumed a structure of such a type for the condensation product obtained from urea and acetylacetone.

This production of a pyrimidine by the action of urea upon nitromalonic aldehyde is attended, therefore, with difficulty and by only small yield. In marked contrast are the condensations carried out by Pinner between β-diketones and amidines. Accordingly, it seemed advisable to try the action of amidines upon nitromalonic aldehyde with a view to studying the influence and rôle which the imino group might play in these reactions.

Benzamidine in the form of its hydrochloride was introduced into an aqueous solution of sodium nitromalonic aldehyde. From this mixture a white crystallin precipitate was thrown down almost immediately, even without the presence of a condensing agent. The product, quantitative in yield, showed the presence of neither hydroxyl nor aldehyde group, but accorded through analyses with a true pyrimidine a 5-nitro-2-phenylpyrimidine (VI). The reaction must have proceeded in accordance with the following scheme:

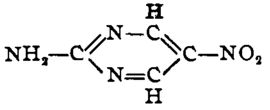

(VI)

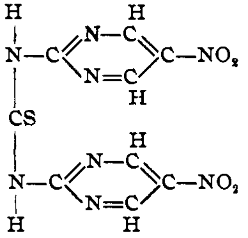
An intermediate compound, as represented above by the condensation between the amino group and one aldehyde group, is no doubt first formed; but the imino group almost immediately reacts with the second aldehyde group, in hydrated form, whereby two molecules of water are lost, the first in the ring closing and the second in the appearance of the unsaturated linkage. The constitution of the intermediate product is indeed most favorable for the second reaction. This tendency for the imino group to enter so readily into a condensation with the hydrated aldehyde group, leaving the second hydroxyl to split off with the hydrogen of the adjoining carbon atom, accounts most likely for the speed and facility with which this condensation is found to run.

The presence of one amino group and one imino group upon the same carbon atom of a compound seems therefore to be the most favorable grouping for the pyrimidine formation. That series of compounds known as the amidines presents exactly this arrangement and constitutes therefore the best possible basis for pyrimidine formation. No matter what other group may be associated with the amidine nucleus, $-C(:NH).(NH_2)$, this tendency to enter into condensation with β-ketonic derivatives should be apparent. From the study of urea it has already been noted with what difficulty the pyrimidine ring is formed when two amino groups in this same position are concerned. The presence therefore of a second amino group in conjunction with the amidine nucleus should not interfere with the ease by which the amidine grouping could enter into condensation. Such a compound is guanidine and by its use in this connection, we should ascertain at once the correctness of this view. With nitromalonic aldehyde guanidine should give a nitroaminopyrimidine. Otherwise, if the two amino groups enter preferably into the reaction, as may well be inferred from the study of urea, we should obtain a nitroiminopyrimidine.

Upon bringing guanidine and nitromalonic aldehyde together, in an aqueous solution, the solution took on a red color at once and a colorless, needle-like, crystallin substance was precipitated—even without a condensing agent. The yield, however, may be made quantitative by use of piperidine as the condensing agent. The product thus obtained gave an affirmative test for the presence of an amino group (carbylamine reaction) and a negative test for the presence of an imino group (Liebermann's nitrosamine reaction). From these and other tests no question remains but that the product contains only the amino group, and this in the 2-position in the pyrimidine ring. Analysis accorded with the formula (VII) a 5-nitro-2-aminopyrimidine.

(VII)





(VIII)

Attempts to prepare the hydrochloride of this nitroaminopyrimidine were unsuccessful. This failure is no doubt due to the strongly negative nature of the nitropyrimidine, and again to the resistance afforded to any substituent upon a carbon atom of a ring situated between two nitrogen atoms. There is, therefore, no tendency for an aminic nitrogen in such position to become basic. On the other hand, an acyl derivative of the amino group is possible, as shown by the preparation of a monoacetylaminopyrimidine by the action of acetic anhydride upon the aminopyrimidine.

When this aminopyrimidine is warmed in carbon disulfide with the presence of a small amount of alkali, a yellow, oily mass is precipitated. This, upon digestion in alcohol, soon solidifies to a yellow crystallin compound—a characteristic property of thio compounds. Analysis showed the substance to be a 5,5'-dinitro-2,2'-dipyrimidylthiocarbamide (VIII).

Hot dilute alkali dissolves the 5-nitro-2-aminopyrimidine but does not attack it. When boiled, however, with a highly concentrated alkaline solution, this pyrimidine is slowly attacked and ammonia set free from the deep red mixture. The solution then contains the 5-nitro-2-hydroxypyrimidine, which can be precipitated out in the form of its silver salt. The free hydroxypyrimidine obtained from the silver salt is in all respects identical with the hydroxypyrimidine procured by the action of urea upon nitromalonic aldehyde. This hydrolysis proves conclusively that the amino group in the pyrimidine must occupy the same relative position as the hydroxyl group in the product from urea, *i. e.*, the 5-nitro-2-hydroxypyrimidine.

The condensation of urea with nitromalonic aldehyde has proceeded only through the formation of a monoureide. An excess of urea seemed in no way to favor the possible formation of a diureide. In order to change the conditions as much as possible it was decided to employ also certain monoalkyl- or arylureas. Such, for example, as methylurea, benzylurea, or phenylurea. In all of these cases only the monoalkyl- or arylureide of nitromalonic aldehyde was procured. The reaction with benzylurea has appeared somewhat more rapid than with the others.

The presence in these substituted ureas of a secondary nitrogen might also have indicated the possibility of a ring formation involving the free aldehyde group of the alkylated monoureide, in similar manner to that displayed by the imino groups of the amidines. As no compounds of the pyrimidine class were obtained, there remains only the conclusion that it is the imino group itself and not a secondary nitrogen atom which serves so well under these conditions for the pyrimidine ring synthesis.

Experimental Part.

Nitromalonic Aldehyde Monoureide, $C_3H_3NO_3(:N.CO.NH_2)$ (I).—Equimolecular quantities of urea (1.2 grams) and sodium nitromalonic aldehyde (3 grams) were brought together in aqueous solution (30 cc.), and a few drops of piperidine added as condensing agent. Two or 3 cc. of N sodium hydroxide solution serve here equally as well. After 24–36 hours the deep red reaction mixture was acidified with dilute sulfuric acid, upon which a light yellow crystallin precipitate immediately formed. Upon filtering off this monoureide, 1 gram in weight, the mother liquor yielded, in the course of 48 hours or more, 0.2 gram of a second precipitate somewhat more granular and less crystallin than the first. This product is the pyrimidine.

The monoureide thus obtained, and purified by crystallization from alcohol, melted at 154° (cor.). It is readily soluble in alcohol, acetic ester or acetic acid; only fairly soluble in acetone or water; and insoluble in chloroform, ether, benzene, carbon disulfide or carbon tetrachloride. It slowly undergoes decomposition and cannot therefore be preserved for any length of time.

Calculated for $C_4H_5N_3O_4$: C, 30.20; H, 3.17; N, 26.46
Found: C, 30.40; H, 3.40; N, 26.82

Sodium Salt of Nitromalonic Aldehyde Monoureide.—The sodium salt was easily prepared by adding sodium ethylate to an alcoholic solution of the monoureide. The salt is deposited as a light brown precipitate, slightly soluble in alcohol, but readily soluble in water. It decomposes violently upon warming. The salt analyzed was purified by crystallization from dilute alcohol. All of its water of crystallization is lost over sulfuric acid.

Calculated for $NaC_4H_4N_3O_4.3H_2O$: H_2O, 22.97; Na, 9.77
Found: H_2O, 22.84, 23.87; Na, 10.86, 9.61

Nitromalonic Aldehyde Ureide-Anil, $C_3H_3NO_2(:N.C_6H_5)(:N.CO.NH_2)$ (IV).—When the monoureide and aniline, in equimolecular quantities, were brought together in a warm alcoholic solution, nitromalonic aldehyde monanil, m. p. 144°, was formed.[1] The ureide group is thus seen to be readily displaceable by aniline. If, however, equimolecular quantities of nitromalonic aldehyde monanil and urea are dissolved in alcohol and a current of dry hydrogen chloride led into the solution till saturation is reached, there appears, upon cooling, a precipitate of glistening, red, needle-like crystals. This substance is the ureide-anil, easily purified by crystallization from alcohol and melting at 211° (cor.). This ureide-anil is readily soluble in chloroform, acetone or benzene; slightly soluble in alcohol, carbon tetrachloride, water or acetic ester; and insoluble in ether or ligroin.

0.1752 gram of substance gave 0.3260 gram CO_2 and 0.0720 gram H_2O.

Calculated for $C_{10}H_{10}N_4O_3$: C, 51.26; H, 4.30
Found: C, 51.93; H, 4.70

Nitromalonic Aldehyde Ureide-Oxime, $C_3H_3NO_2(:NOH)(:NCO.NH_2)$ (III).—The monoureide was introduced into a solution containing the calculated amount of hydroxylamine hydrochloride (1 mol.) and just sufficient alkali added for neutralization. A yellow leaf-like crystallin precipitate appeared on short standing. This product is the monoureide-oxime. It is somewhat soluble in alcohol, acetone, acetic ester or acetic acid; insoluble in chloroform, ether, benzene or ligroin. When recrystallized from alcohol it melted at 174–5° (cor.).

Calculated for $C_4H_6N_4O_4$: C, 27.58; H, 3.47
Found: C, 27.52; H, 4.11

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[1] *Am. Chem. J.,* **22,** 99 (1899).

Attempts to prepare the monoureide-phenylhydrazone were unsuccessful. In all cases urea was split off from the nitromalonic aldehyde monoureide and replaced by the phenylhydrazine radicle, whereby the 1-phenyl-4-nitropyrazole, as previously mentioned, was formed by intramolecular condensation.

The ease with which urea is eliminated from this nitromalonic aldehyde monoureide by means of aniline or phenylhydrazine made possible a simple determination of the urea per molecule of product. To an alcoholic solution of the monoureide the theoretical amount of aniline was added, and the solution then titrated against a solution of mercuric nitrate. In this method of Liebig the mercuric nitrate solution was made up so that 1 cc. was equivalent to 0.07 gram HgO and about equivalent to 0.01 gram urea.

Calculated for $C_4H_5N_3O_4$: 1 mol. urea 37.74%; found, 35.10%

5-Nitro-2-hydroxypyrimidine, $C_4H_3N_3O_2$ (II).—This product appears in the course of a few hours' standing of the mother liquor left after the removal of nitromalonic aldehyde monoureide previously described. The formation is continuous for two or three days, but only in very small quantities. It appears in small yellow plates, of a deeper color than the monoureide, and is insoluble in water, carbon disulfide, ether, chloroform, carbon tetrachloride, ligroin or benzene; sparingly soluble in acetone, acetic ester or alcohol and only slightly soluble in hot acetic acid or its anhydride. It may be recrystallized, but with difficulty, from glacial acetic acid; the m. p. is 203.5° (cor.).

Calculated for $C_4H_3N_3O_3$: C, 34.03; H, 2.14; N, 29.80
Found: C, 33.92; H, 2.40; N, 29.69

When 1.2 grams of sodium nitromalonic aldehyde and 0.3 gram urea were brought into reaction, the mother liquor, left after the removal of the monoureide within a few minutes after the acidification, scarcely ever yielded more than 0.2 gram pyrimidine, *i. e.*, 18% of the theoretical.

By far the larger portion of the product in this reaction consists of the monoureide, from 70–80% of theoretical yield. Experiments, therefore, which might lead to a further condensation in the molecule of this ureide were extensively pursued. When the monoureide is dissolved in acetic anhydride and anhydrous hydrogen chloride led into the solution, there appeared upon cooling a small quantity of the pyrimidine, 10–15% of the theoretical yield. An excess of dilute sulfuric acid added to the reaction-mixture of nitromalonic aldehyde and urea suffices to increase the yield in pyrimidine, providing that the mixture is kept near 50°. On the other hand the action of dilute sulfuric acid upon the free monoureide in aqueous suspension, even when warmed, is not as effective. When heated in sealed tubes with acetic anhydride, either alone or in the presence of zinc chloride, anhydrous sodium acetate or phosphorus pentoxide, the monoureide underwent decomposition, whereas the use of similar agents in the same solvent at room temperature was ineffective altogether.

Sodium Salt of 5-Nitro-2-hydroxypyrimidine.—The sodium salt of this pyrimidine may be prepared in fair yield by warming an alcoholic solution of the monoureide with excess of sodium ethylate over a water bath for several hours. The sodium salt of the pyrimidine is less soluble in alcohol than that of the monoureide, consequently it is found to separate out almost as fast as formed. This sodium salt was obtained in 10–15% yield. When recrystallized from water the red crystals accorded with the following analyses:

Calculated for $NaC_4H_2N_3O_3.2H_2O$: H_2O, 18.59; Na, 11.56
Found: H_2O, 17.82; Na, 12.38

Potassium Salt of 5-Nitro-2-hydroxypyrimidine.—In a similar manner to that for the preparation of the sodium salt, the potassium salt may be obtained by use of potassium ethylate. Or, if desired, potassium hydroxide may be used to dissolve the free pyrimidine and the neutral deep red solution evaporated to the point of crystallization, when the yellow prismatic crystals of the potassium salt come out.

Calculated for $KC_4H_2N_3O_3.H_2O$: H_2O, 9.14; K, 19.80
Found: H_2O, 8.99; K, 19.60

Barium Salt of 5-Nitro-2-hydroxypyrimidine.—When the pyrimidine is dissolved in ammonium hydroxide and barium hydroxide added to this neutral solution, a reddish brown precipitate of the barium salt is thrown down. This salt lost all of its water of crystallization at 110°.

Calculated for $BaC_8H_4N_6O_6.4H_2O$: H_2O, 14.73; Ba, 24.08
Found: H_2O, 13.30; Ba, 24.04

Silver Salt of 5-Nitro-2-hydroxypyrimidine.—The silver salt was prepared by adding a solution of silver nitrate to one of the ammonium salt of the pyrimidine. It is of a reddish yellow color and only slightly soluble in water.

Calculated for $AgC_4H_2N_3O_3$: Ag, 43.55; found, 43.10

5-Nitro-2-methoxypyrimidine, $C_4H_2N_2(NO_2).(OCH_3)$ (V).—The dried sodium salt of the hydroxypyrimidine, suspended in absolute alcohol, was warmed with methyl iodide, under reflux condenser, for two or three hours. The mixture was then evaporated to dryness over a water bath and the residue extracted with benzene. The yield is very poor. After several recrystallizations from benzene the pure product melted at 168–9° (cor.). Upon repeated melting and recooling the ether always gave this same melting point, indicating therefore no tendency for transformation or wandering of the methoxyl group. It is a colorless, plate-like crystallin substance, readily soluble in benzene; fairly soluble in alcohol, but insoluble in ether.

Calculated for $C_5H_5N_3O_3$: C, 38.69; H, 3.25
Found: C, 38.86; H, 3.49

A determination of the position of the methoxyl group in this ether was carried out in accordance with the method of Zeisel. The ether was placed in a small flask, containing also a solution of hydriodic acid and ammonium iodide and warmed very gently. The methyl iodide evolved was led through a series of flasks containing hydriodic acid, water, and moist red phosphorus in order, and finally into one containing a diluted alcoholic solution of silver nitrate. A temperature of only 40° was found sufficient to decompose the ether and liberate all of the methyl iodide, which was to be determined as silver iodide in the last of the flasks, just mentioned. This low temperature (usually given as between 40° and 80° for such determinations) indicates that we have the methoxyl group attached to a carbon atom and not to a nitrogen in the pyrimidine ether.

Calculated for $C_5H_5N_3O_3$: CH_3, 9.68%; found, 7.99%.

Many attempts were made toward effecting a reduction of the free nitrohydroxypyrimidine, but decomposition interfered in all cases.

5-Nitro-2-phenylpyrimidine, $C_4H_2N_2(NO_2).C_6H_5$ (VI).—Equimolecular quantities of benzamidine hydrochloride and sodium nitromalonic aldehyde, when brought together in aqueous solution, gave a white flocculent precipitate almost immediately. The presence of sodium hydroxide as a condensing agent was found to retard somewhat this precipitation, but by acidification the total yield (practically quantitative) could be realized. Consequently, the sodium salt of the intermediate product necessarily formed in this condensation must have undergone an immediate hydrolysis. The pyrimidine is fairly soluble in alcohol, ether, or benzene, but insoluble in water. The product was best purified by crystallization from an alcohol and ether solution. The soft white plates gave a melting point of 219° (cor.).

Calculated for $C_{10}H_7N_3O_2$: C, 60.00; H, 3.51; N, 20.89
Found: C, 60.17; H, 3.78; N, 20.82

5-Nitro-2-aminopyrimidine, $C_4H_2N_2(NO_2).(NH_2)$ (VII).—When equimolecular quantities of guanidine carbonate and sodium nitromalonic aldehyde were mixed in aqueous solution there appeared immediately a flocculent white precipitate. The yield was made almost quantitative by use of a few drops of piperidine as condensing agent. The product is soluble in alkali and reprecipitated by addition of acid. It is soluble in acetone, alcohol or acetic ester; fairly soluble in water; insoluble in ether, ligroin, chloroform, benzene or carbon tetrachloride. Recrystallized from alcohol, the fine, colorless needles melted at 236° (cor.).

Calculated for $C_4H_4N_4O_2$: C, 34.27; H, 2.87; N, 40.01
Found: C, 34.00; H, 2.59; N, 40.17

The presence of a free amino group in this pyrimidine was confirmed by several qualitative tests, such, for example, as the "carbylamine" reaction with alcoholic potassium hydroxide. The Hinsberg test with benzene sulfochloride gave only a clear solution and no oily product as is obtained with compounds containing the imino group. Upon addition of sodium nitrite to an acid solution of this pyrimidine the absence of an oily product further confirmed the absence of an imino group (Liebermann).

When the aminopyrimidine is boiled with alkali, a rapid evolution of ammonia is detected. In fact ammonium hydroxide itself is sufficient for this hydrolysis. When a solution of the aminopyrimidine in concentrated ammonium hydroxide is boiled till no further odor of ammonia is noted, and silver nitrate then added to the deep red solution, there appeared a reddish brown precipitate of a silver salt which proved to be the silver salt of 5-nitro-2-hydroxypyrimidine.

Calculated for $AgC_4H_2N_3O_3$: N, 16.93; Ag, 43.55
Found: N, 16.60; Ag, 41.35, 43.36

This silver salt of the 5-nitro-2-hydroxypyrimidine, as prepared from the aminopyrimidine, was next heated in aqueous suspension with hydrochloric acid and the clear solution filtered from the silver chloride thus formed. Upon evaporation to small bulk, the light yellow, semicrystalline hydroxypyrimidine made its appearance, in all respects identical with the hydroxypyrimidine prepared from urea and nitromalonic aldehyde. By the action of methyl iodide upon this silver salt suspended in absolute methyl alcohol, at the temperature of a water bath, there was obtained, in like manner to the process already described, the same identical 5-nitro-2-methoxylpyrimidine prepared by the action of methyl iodide upon the silver salt of the hydroxypyrimidine obtained from urea.

When the aminopyrimidine was warmed with a slight excess of an approximately normal sodium hydroxide solution, until the odor of ammonia was no longer apparent, and this deep red solution evaporated with much care upon a water bath, the reddish-brown crystals of the sodium salt of the hydroxypyrimidine came out. An analysis showed that the product contained two molecules of water of crystallization and was in all respects identical with the sodium salt of the hydroxypyrimidine previously described.

5-Nitro-2-acetylaminopyrimidine, $C_4H_2N_2(NO_2).(NHCOCH_3)$.—The acetyl derivative was obtained by warming the aminopyrimidine with an excess of acetic anhydride in presence of anhydrous sodium acetate. The solution was heated for a period of three hours upon the steam bath, after which, upon cooling, the acetyl compound crystallized out in beautiful, long, colorless needles. The yield amounted to 80% of the theoretical. The product is readily soluble in acetic acid, benzene, alcohol or chloroorm; slightly soluble in water, carbon tetrachloride, acetic ester or acetone;

and insoluble in ether or ligroin. When purified by recrystallization from alcohol it melted at 172.5° (cor.).

Calculated for $C_6H_6N_4O_3$: N, 30.86; found, 30.84

Attempts to prepare the hydrochloride of the 5-nitro-2-aminopyrimidine were unsuccessful. Various acids were employed in this connection to ascertain what amino salt might be formed, but in no case could any action be detected. This amino group is thus shown to be very resistent.

5,5'-Dinitro-2,2'-dipyrimidyl Thiocarbamide (VIII), $CS(NH.(C_4H_2N_2.NO_2))_2$.—When 5-nitro-2-aminopyrimidine was suspended in carbon disulfide and a small amount of potassium hydroxide added to this mixture, kept at 60°, a yellow, oily mass collected after a short time at the bottom of the vessel. Upon removal this product was digested with alcohol and soon passed over into a mass of glistening leaflets. This thio-compound is soluble in alcohol, carbon disulfide or acetic ester; fairly soluble in water or ether; slightly soluble in acetone, chloroform or benzene; insoluble in ligroin or carbon tetrachloride. Recrystallized from alcohol the pure product melted at 230–1° (cor.). Attempts to liberate the aminopyrimidine from this thio-compound were unsuccessful. Decomposition took place in all cases.

Calculated for $C_9H_6N_8O_4S$: N, 34.78; found, 34.36

Nitromalonic Aldehyde Monophenylureide, $CHO.CH(NO_2)CH : N.CO.NH.C_6H_5$.—Equimolecular quantities of nitromalonic aldehyde and phenylurea were brought together in alcoholic solution and a few drops of piperidine added. Though a portion of the product is precipitated in a short time, the solution must be acidified to effect a complete separation of the free substance. This monophenylureide is soluble in alcohol or ether but insoluble in water. Recrystallized from alcohol it melted at 176–7° (cor.).

Calculated for $C_{10}H_9N_3O_4$: C, 51.06; H, 3.86
Found: C, 49.80; H, 4.10

Nitromalonic Aldehyde Monobenzylureide, $CHO.CH(NO_2).CH : N.CO.NH.CH_2C_6H_5$.—When benzylurea and nitromalonic aldehyde were brought together in alcoholic solution in the presence of a few drops of piperidine, a condensation took place almost immediately, as noted by the deepening in red color of the solution. Upon acidification the colorless leaflets of the free benzylureide were thrown down. This product is soluble in alcohol, chloroform, acetone or acetic ester; insoluble in benzene, carbon tetrachloride or ligroin. Recrystallized from alcohol it melted at 150–1° (cor.).

Calculated for $C_{11}H_{11}N_3O_4$: N, 16.86; found, 16.18

Nitromalonic Aldehyde Monomethylureide, $CHO.CH(NO_2).CH : N.CO.NHCH_3$.—This product was prepared by bringing together monomethylurea and nitromalonic aldehyde in aqueous solution. After the addition of a few drops of piperidine the color of the solution indicated the completion of the reaction in about one day. Upon acidification, the yellow crystals of the monomethylureide were precipitated. This product is soluble in alcohol or acetone; fairly soluble in chloroform, acetic ester or ligroin; insoluble in ether, benzene or carbon tetrachloride.

Calculated for $C_5H_7N_2O_4$: C, 34.64; H, 4.04
Found: C, 34.84; H, 3.88

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[CONTRIBUTION FROM THE CHEMICAL RESEARCH LABORATORY, SECTION OF AGRONOMY, IOWA AGR. EXPT. STA.]

THE CHEMICAL NATURE OF THE ORGANIC NITROGEN IN THE SOIL.

[SECOND PAPER.]

BY S. L. JODIDI.

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By applying the Hausmann-Osborne[1] method, as well as the formaldehyde[2] titration method perfected by Sörensen, the writer[3] has demonstrated that the acid-soluble organic nitrogen occurring in Iowa soils and in Michigan peat soils is made up chiefly of acid amides, monoamino acids and diamino acids. In the meantime, and in part before those publications, there appeared several papers dealing with the isolation of organic nitrogenous compounds from soils. Thus, Schreiner and Shorey succeeded in isolating from various soils the diamino acids arginine[4] and histidine, as well as the pyrimidine[5] derivative, cytosine, and the purine[6] bases, xanthine and hypoxanthine. Prior to that Shorey extracted from Hawaiian soils a compound which he identified as picolinecarboxylic acid.[7] Among the decomposition products of Michigan peat the monoamino acids leucine[8] and isoleucine were isolated and identified by Robinson, who also quantitatively determined the amino[9] nitrogen in the peat by Van Slyke's[10] nitrous acid method.

Adding, as the above researches do, to our knowledge concerning the nature of organic compounds in soils, yet it seems desirable, if not im-

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[1] *Z. physiol. Chem.*, 27, 95 (1899); 29, 47 (1900); 29, 136 (1900); 31, 215 (1900). THIS JOURNAL, 25, 323 (1903).

[2] *Biochem. Z.*, 7, 47(1907); 7, 407 (1908).

[3] THIS JOURNAL, 32, 396 (1910); 33, 1226 (1911). *Technical Bull.* 4, (1909) Mich. Agr. Exp. Sta.; *Research Bull.* 1, (1911) Iowa Agr. Exp. Sta.

[4] *J. Biol. Chem.*, 8, 381 (1910).

[5] *Ibid.*, 8, 385 (1910). *Bull.* 74, Bureau of Soils, U. S. Dept. Agr.

[6] *Ibid.*

[7] Ann. Rept. of Hawaii Agr. Exp. Sta., 1906, p. 55.

[8] THIS JOURNAL, 33, 564 (1911).

[9] Michigan Agr. Expt. Sta., *Techn. Bull.* 7, p. 11.

[10] *Ber.*, 43, 3170 (1910).