Experimental

Reaction of Ethylamine-1-C^{14} with Nitrous Acid.—An aqueous solution of ethylamine-1-C^{14} was prepared from sodium cyanide-C^{14} (100 μcuries of C^{14}) by the procedure of Kilmer and du Vigneaud[14] on a 0.23-mole scale. About 40% of the reduction mixture was acidified with hydrochloric acid, diluted with 6.1 g. of ethylamine hydrochloride and evaporated almost to dryness under reduced pressure. The residue was treated with excess 20% sodium hydroxide solution and steam distilled until all of the ethylamine was removed. The steam distillate was titrated with dilute perchloric acid (0.112 eq., 68%) to *p*H 4. The solution was cooled to 3° and 23 g. (0.34 mole) of sodium nitrite in 50 ml. added rapidly. After one-half hour, the mixture was heated at 50° for an hour and then distilled slowly for 2.5 hours. The ethylene which was evolved during the reaction was absorbed in a gas washing bottle equipped with a fritted disk and containing liquid bromine at 10°. During the distillation, the last of the ethylene was swept out of the system into the trap with a stream of nitrogen. The recovery of ethylene as the dibromide was 1.1 g. after purification by distillation.

The aqueous distillate was neutralized and steam distilled. The distillate was saturated with potassium carbonate and continuously extracted with ethanol-free diethyl ether for three days. The extract was dried over magnesium sulfate and fractionated. The yield of ethanol, b.p. 77–78°, was 1.94 g. (38%). Part of the material was converted to the 3,5-dinitrobenzoate, m.p. 92.5–92.8°, for C^{14}-assay.

The labeled ethanol was degraded as follows. A solution of 0.5 g. of ethanol-C^{14} in 30 ml. of water was treated simultaneously with 10% sodium hydroxide and iodine–potassium iodide solutions (100 g. of potassium iodide, 50 g. of iodine in 400 ml. of water) at 50° until a persistent iodine color was obtained. The mixture was poured into ice-water, the iodoform collected and crystallized twice from ethanol–water, m.p. 118° (dec.).

A check degradation was performed on ethanol-1-C^{14} obtained by lithium aluminum hydride reduction of acetic-1-C^{14} acid prepared as described earlier.[15]

The radioactivity analyses are given in Table I.

Action of Nitrous Acid on Ethylene-C^{14}.—The ethylene dibromide obtained above was converted back to ethylene by the action of zinc powder in boiling ethanol then mixed with nitrogen and passed ten times through a fritted disk immersed in a solution at 60° containing 1.2 g. (0.017 mole) of sodium nitrite, 11.2 ml. of 1.57 *N* perchloric acid (0.018 mole) and 1.23 g. of ordinary ethanol over a period of an hour. The ethanol in the reaction mixture was isolated as described above and converted to the 3,5-dinitrobenzoate for C^{14}-assay. For comparison, the ethanol used as a carrier was also assayed (Table I). The ethylene used amounted to 0.0049 mole (activity of 1180 dis./min./labeled C-atom) and if it were all hydrated the recovered ethanol would be expected to have an activity of 180 dis./min./labeled C-atom. Since the recovered ethanol did not have an activity significantly different from the carrier ethanol it is unlikely that any hydration occurred under the reaction conditions.

Reaction of Ethylamine with Nitrous Acid in Deuterium Oxide.—Ethylamine hydrochloride (9.3 g., 0.11 mole) was dissolved in 120 ml. of water and treated with 30 ml. of 20% sodium hydroxide solution. The liberated ethylamine was steam distilled, the distillate neutralized with perchloric acid and evaporated to dryness under reduced pressure. After one hour at room temperature at 1 mm., 2 ml. of 99.8% deuterium oxide[16] was added and the mixture allowed to stand for 0.5 hour. The water was removed under reduced pressure as before and the residue dissolved in 40 ml. of 99.8% deuterium oxide. Sodium nitrite (23 g., 0.34 mole) was added and the balance of the reaction and isolation of the products were carried out as described above. The yield of ethanol was 1.2 g. (45%). The product was converted to the 3,5-dinitrobenzoate for deuterium analysis which was carried out by combustion and assay of the resulting water by the "falling-drop" procedure. The ester contained 0.70 atom % deuterium which after correction for the hydrogens of benzene ring gave 1.1 atom % deuterium for the hydrogens bound to carbon in the ethanol.

Cambridge 39, Massachusetts

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[14] G. W. Kilmer and V. du Vigneaud, *J. Biol. Chem.*, **154**, 247 (1944).

[15] J. D. Roberts, D. R. Smith and C. C. Lee, This Journal, **73**, 618 (1951).

[16] Obtained on allocation by the U. S. Atomic Energy Commission.

[Contribution from the Noyes Chemical Laboratory, University of Illinois]

Malonyl-α-aminopyridine. II. Hydrolysis of its Diazonium Coupling Products and Related Compounds[1]

By H. R. Snyder and Michael M. Robison[2]

Received July 9, 1952

Diazonium coupling products (II) derived from malonylaminopyridine decompose in the presence of dilute aqueous base, even at room temperature, in an unexpected fashion. The primary products are carbonic and hydrocyanic acids, α-pyridyl isocyanate and aromatic amines. The acids mentioned are produced as salts, at least in part; the pyridyl isocyanate undergoes further hydrolysis to α-aminopyridine, which reacts with the isocyanate to give the dipyridylurea; the aromatic amines formed also react with the pyridyl isocyanate to produce unsymmetrical ureas. Certain other compounds that are closely related to the coupling products decompose in the same fashion. The limitations of the reaction are explored and mechanisms are discussed.

In attempts to effect the purification of the product (IIa) obtained[1] by the Japp–Klingemann reaction of benzenediazonium chloride with malonylaminopyridine (I), water was employed as a recrystallization solvent. A white crystalline solid, rather than the colored coupling product, was obtained, indicating that hydrolysis had occurred. The analysis of the hydrolysis product corresponded to the empirical formula $C_{12}H_{11}N_3O$. By analogy to the path[1] taken in the reaction of alcohols with molecules of type II, *i.e.*, the cleavage of the central amide linkage to yield esters of type III (*vide infra*), it seemed not unlikely that a parallel hydrolysis might have taken place, with subsequent decarboxylation of the acid to yield the phenylhydrazone of N-(α-pyridyl)-glyoxylamide (IV). This compound, however, is of the empirical composition $C_{13}H_{12}N_4O$, which differs from that of the actual hydrolysis product by the elements of hydrogen cyanide. A test on the gases evolved from the hydrolysis mixture showed that hydrogen cyanide was formed, and an independent synthesis proved that the white product was N-phenyl-N'-

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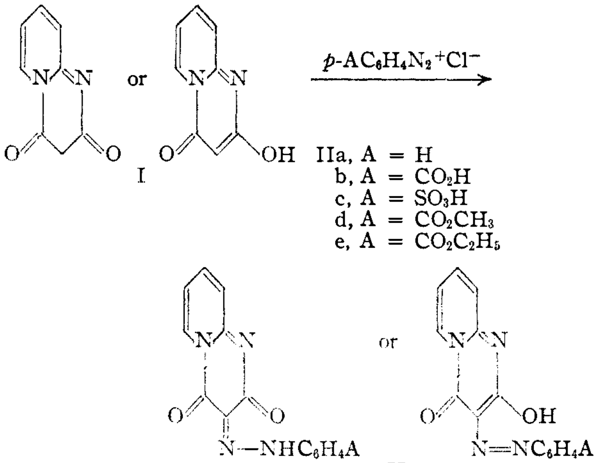
[1] For preceding paper in this series see H. R. Snyder and Michael M. Robison, This Journal, **74**, 4910 (1952).

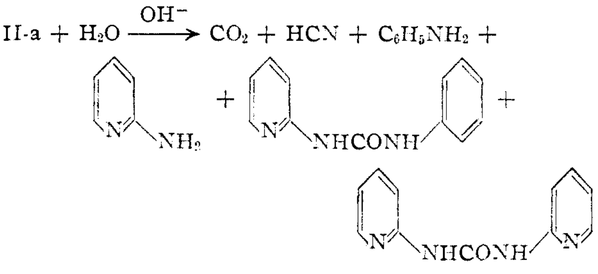
[2] Allied Chemical and Dye Corporation Fellow, 1951–1952.


I

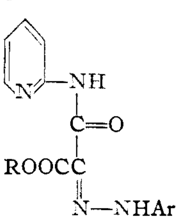
IIa, A = H
b, A = CO_2H
c, A = SO_3H
d, A = CO_2CH_3
e, A = $CO_2C_2H_5$

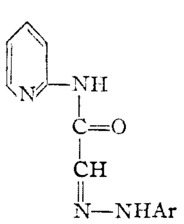
II

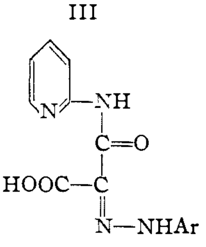
(α-pyridyl)-urea. Other products, as shown below, were also demonstrated.

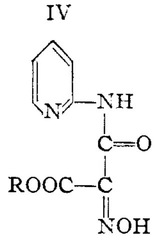


The original experiments were performed with IIa in an impure state, directly as it was isolated from the preparation mixture. It was not realized at the time that the substance is weakly acidic, and that the crude product was contaminated by its potassium salt and other strongly basic ingredients. When it was later shown that the hydrolysis is base-catalyzed, the hot water treatment was repeated with pure IIa. The decomposition was much slower and only a very faint cyanide test was obtained. Furthermore, unlike crude IIa, the pure compound does not slowly generate hydrogen cyanide on storage.


III


IV


V

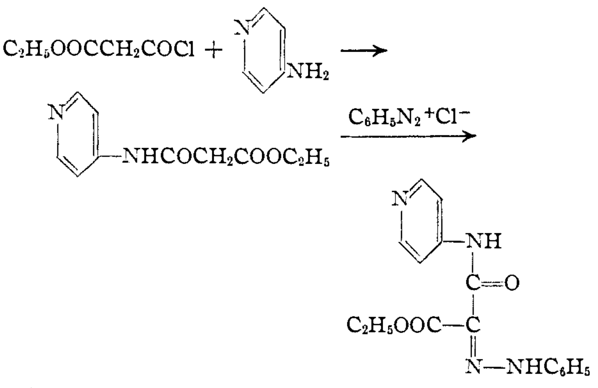

VI

Subsequent investigations of the limitations of the decomposition showed that in the presence of aqueous alkali it may occur with compounds of type II and with substances of the following structures:

1. **Esters of Type** III.—Such substances can be saponified by shaking with a mixture of aqueous sodium hydroxide and methanol, and reprecipitating immediately with acid before further decomposition can take place. The precipitate so obtained appears to be a mixture of the expected acid (V) and the original coupling product (II), as indicated by the infrared spectrum; recrystallization from isopropyl alcohol results in the recovery of the coupling product only, indicating that III or V, or both, may recyclize under the conditions of the experiment. It seems not improbable that cyclization is indeed a preliminary step in the decomposition of all the open-chain compounds, and that II is an intermediate common to them all. This hypothesis is strengthened by the apparent structural limitations on the reaction (*vide infra*) and by the formation of a transitory red color in the basic solutions of the esters during their hydrolysis.

2. **Compound** V.—This substance decomposes either on treatment with aqueous base or on attempted thermal decarboxylation, yielding the same products as are obtained from II.

3. **Oximes of Type VI, Which Are Analogous to** III.—It has been found that the following related compounds do *not* undergo the cleavage when subjected to treatment with alkali. (1) Phenylhydrazones of certain glyoxylic acid derivatives. This limitation includes the derivatives of the anilide and the unsubstituted amide, as well as of esters and of the acid itself. Although the last substance has been reported to evolve some hydrogen cyanide on thermal decomposition,[3] its preparation[4] involves a two-hour reflux period with aqueous alkali. (2) Oximes of certain glyoxylic acid derivatives, including the oxime of *o*-nitroglyoxylanilide. (3) Esters similar to III and VI except that the α-pyridyl group is replaced by some other moiety. An ester of particular interest is ethyl N-(γ-pyridyl)-mesoxalamate phenylhydrazone. This compound, which produced no cyanide ion after standing one week in 3% aqueous sodium hydroxide, was prepared as shown in the equation.



From these studies it seems likely that any compound of the general structure VII, or its cyclization product VIII, will undergo the decomposition. In the open chain compounds (VII) the pyridyl

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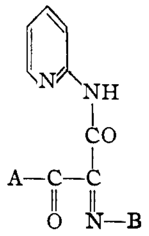
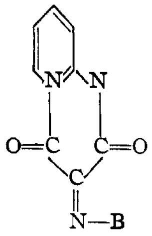
[3] A. Elbers, *Ann.*, **227**, 353 (1885).

[4] M. Busch, F. Achterfeldt and R. Seifert, *J. prakt. Chem.*, [2] **92**, 1 (1915).



VII

A = OH, OR
B = NHAr,
NHR,
OH,
NH_2,
$NHCONH_2$



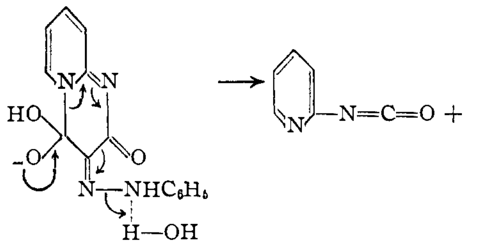
VIII

group attached to the mesoxalamide function must by an α-pyridyl residue, and the group A must be of such a nature that cyclization by reaction with the pyridine nitrogen can occur. It was observed that N-α-pyridyl-N′-*n*-butylmesoxalamide phenylhydrazone did not generate cyanide ion even after standing 15 days in 3% sodium hydroxide solution at room temperature; the failure of the reaction here can be attributed to the stability of the butylamide group (COA). The nitrogen atom carrying B is represented as doubly bonded to the central carbon atom of the mesoxalamic acid residue, since these two atoms are bonded together multiply in the ejected cyanide ion. Although the reaction discussed here appears to be the first recorded hydrolytic fission of the linkage between the nitrogen atoms of a simple phenylhydrazone, a recent investigation by Curtin and Russell[5] disclosed that certain benzoylphenylhydrazones of diphenyltriketone undergo such a fission either under the influence of aqueous base or when absorbed on activated alumina. Auwers[6] has reported a similar reaction of the benzoylphenylhydrazone of *p*-benzoquinone. In these compounds the presence of the acyl group prevents the change of the phenylhydrazone structure to an azo linkage. Consideration of these observations lends weight to the probability that the double bond must be able to occupy the position indicated in VII. The available evidence[1] indicates that the preferred form of compounds of the type II is the azo structure rather than the phenylhydrazone tautomer; possibly cyclic structures like VIII do not exist except as addition products with hydroxide ion.

There are several reasons for believing that α-pyridyl isocyanate is an intermediate in the formation of the ureas isolated from the cleavages. First, when compound IIe (which contained basic impurities from its preparation[1]) was boiled with water to which a small quantity of aniline had been added, N-phenyl-N′-(α-pyridyl)-urea was formed. Similarly, the addition of α-aminopyridine to an aqueous suspension of IIa, and subsequent boiling, produced dipyridylurea. It is thought that this compound is formed in any case from the amine which is present as a result of hydrolysis of part of the isocyanate. That the amine is indeed present was shown in another hydrolysis of IIe. The reaction mixture after heating was made strongly basic, and the solution was treated with benzoyl chloride. From this mixture the dibenzoyl derivative of α-aminopyridine was isolated. Finally, refluxing compound IIa with two moles of sodium methoxide in ordinary methanol (which had not been dried) produced methyl N-(α-pyridyl)-carbamate as the main product (58% yield) as well as hydrogen cyanide. In addition, a 24% yield of compound V was formed, apparently by a parallel route.

If a preliminary cyclization of these compounds is the first step in the decomposition, there are still several possible mechanisms for the remaining steps. In the case of the coupling products it seems necessary to postulate the shift of a hydrogen atom to form a phenylhydrazone from the azo compound. In the mechanisms considered most plausible the next step is the attack by base at the central amide carbonyl group. One series of bond shifts which would account for the subsequent cleavage is shown in sequence A.

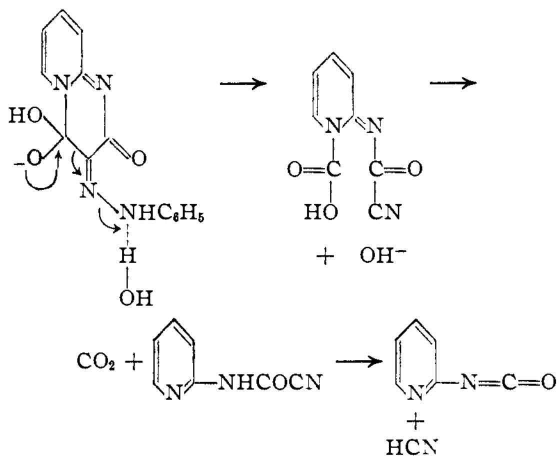
(A)



$C_6H_5NH_2 + OH^- + [HOOCCN] \longrightarrow CO_2 + HCN$

An alternative mechanism which involves cleavage of different linkages is shown in sequence B.

(B)



It may be noted that N-*p*-tolylcarbamyl cyanide is known to decompose rapidly in aqueous sodium hydroxide to form cyanide, carbonate and *p*-toluidine, while in boiling water it forms carbon dioxide, hydrogen cyanide and N,N′-di-*p*-tolylurea.[7]

Experimental[8–10]

I. Hydrolyses of Diazonium Coupling Products

Aniline Coupling Product.—In the first experiments, the crude coupling product (as obtained from the preparation mixture) was boiled with distilled water. Part of the material dissolved, but a dark tarry residue was left. On filtra-

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[5] D. Y. Curtin and C. S. Russell, THIS JOURNAL, **73**, 5450 (1951).

[6] K. Auwers and F. Eisenlohr, *Ann.*, **369**, 209 (1909).

[7] A. Plowman and M. A. Whiteley, *J. Chem. Soc.*, **125**, 587 (1924).

[8] All melting points are uncorrected.

[9] Microanalyses by Miss Emily Davis, Mrs. Jean Fortney, Mrs. Katherine Pih and Mrs. E. Fett. Infrared analyses by Miss Elizabeth Petersen and Miss Helen Miklas.

[10] Preparations of compounds, if not given below, are to be found in reference 1.

tion a quantity of slightly colored crystals was obtained from the pink filtrate. Repeated recrystallizations from 50% aqueous methanol yielded rosettes of white needles of N-phenyl-N'-(α-pyridyl)-urea; m.p. 186.2–187° and 184–187° in two different preparations (reported[11] m.p. 187°).

Anal. Calcd. for $C_{12}H_{11}N_3O$: C, 67.59; H, 5.20; N, 19.71. Found: C, 67.44, 67.34; H, 5.33, 5.22; N, 19.44, 19.89. (Above two samples.)

In one experiment the residue was repeatedly extracted with fresh portions of boiling water, the extracts were combined and evaporated to a small volume, and the urea was collected; from 1 g. of crude coupling product 0.2 g. (25%) of crude urea was obtained.

The effect of alkaline catalysts was demonstrated in an experiment in which the pure coupling product,[1] m.p. 246–246.4°, recrystallized from isopropyl alcohol, was boiled with water in an apparatus connected to an aqueous alkali trap. After several minutes, the amount of cyanide in the trap was hardly sufficient for a positive prussian blue test. In comparable experiments with the crude coupling product, the presence of cyanide was unmistakable. At the end of the experiment with the pure material the residual mixture was made alkaline with a few drops of sodium hydroxide and set aside; when it was subjected to the prussian blue test three days later, a strongly positive reaction was observed.

In another experiment, the coupling product was partially purified by washing it with dilute aqueous acetic acid after the preparation (to remove its potassium salt and other basic impurities) and then extracting it with boiling isopropyl alcohol. It was found that this latter treatment had the effects of thoroughly drying the substance and purifying it sufficiently to prevent decomposition on storage, while at the same time obviating the necessity for recrystallization from this solvent, in which its solubility is inconveniently slight. The solid obtained by this procedure melted at 238° dec. (m.p. of pure substance 246° dec.[1]). When 0.01 mole of this compound was heated for two hours at 100° with 0.01 mole of potassium hydroxide in 50 ml. of water, 1.2 g. (56.3%) of the urea, m.p. 187.5–188.5°, was obtained. On admixture with authentic material the melting point was 186.5–187.5°.

Independent Synthesis of the Urea.—Phenyl isocyanate (11.9 g., 0.1 mole) was added directly to 9.4 g. (0.1 mole) of α-aminopyridine. When the violent reaction had subsided, the mixture was heated on the steam-bath for one-half hour. On recrystallization of the white solid from alcohol, white needles, m.p. 187–188°, were obtained. On admixture with the second analytical sample from above (m.p. 184–187°) a melting point of 185–186.6° was observed. The infrared spectra were identical in all respects.

Di-α-pyridylurea.—The aniline coupling product IIa (2 g.), was boiled with 200 ml. of water which contained 2 g. of α-aminopyridine. The crystals obtained from the filtrate were recrystallized once from 50% aqueous methanol, the product (largely phenylpyridylurea) was discarded, and the mother liquors were evaporated to a small volume. On cooling, a solid, m.p. 166–171°, separated. This was found to be a mixture which was rich in dipyridylurea. Since the compound would have been difficult to separate in the pure state, its presence was demonstrated by comparison of the infrared spectrum of this material with that of a synthetic mixture (m.p. 177–179°) of the two ureas, which was prepared by recrystallizing the authentic compounds together.[12] The spectra of the two mixtures were qualitatively identical; a larger proportion of the dipyridyl compound was present in the lower-melting mixture.

Hydrogen Cyanide and Carbon Dioxide Formation.—When product IIa (crude, slightly alkaline) was boiled with water in a flask carrying a tube leading to a container of barium hydroxide solution, a heavy white precipitate formed; this solid dissolved with effervescence in dilute hydrochloric acid. When the outlet tube was led into dilute sodium hydroxide solution for several minutes, sodium cyanide was formed, as evidenced by strong positive prussian blue tests.

Isolation of a Derivative of α-Aminopyridine.—Crude compound IIe (3 g., containing basic impurities from its preparation) was boiled with 150 ml. of distilled water, and the mixture was filtered. On cooling, a small quantity of tarry solid precipitated from the filtrate.[13] Filtration, followed by treatment with potassium hydroxide and benzoyl chloride, produced a pink precipitate, the dibenzoyl derivative of α-aminopyridine. Recrystallization from alcohol yielded white needles; m.p. 168.2–170° (reported[14] m.p. 166–167°). An authentic sample of the derivative, m.p. 168–170° (prepared[14] from Eastman Kodak Co. white label α-aminopyridine) when mixed with the above compound, melted at 168.2–170°.

Reaction of IIe with Water and Aniline.—Compound IIe (2 g. containing basic impurities from its preparation), was boiled with a mixture of 100 ml. of water and 2 ml. of aniline. From the filtrate was obtained an orange, base-insoluble precipitate. Several recrystallizations from 50% aqueous methanol (Darco) produced white needles, m.p. 188–188.5°. On admixture with an authentic sample of N-phenyl-N'-(α-pyridyl)-urea (m.p. 187–188°) a melting point of 188–188.5° was observed.

Hydrolysis of Other Coupling Products of Type II.—A mixture of IIb with dilute hydrochloric acid gave no indication of the presence of cyanide ion after six days at room temperature in a closed flask. A strongly positive test was obtained after one day in the presence of dilute ammonium hydroxide. Compounds IIc, IId and IIe all generated cyanide, as indicated by the prussian blue test, when allowed to stand with dilute aqueous alkali.

II. Hydrolyses of Esters

Methyl N-(α-Pyridyl)-mesoxalamate Phenylhydrazone.—This substance, after standing two days in 10% aqueous sodium hydroxide, gave a positive prussian blue test. In another experiment 1.5 g. of the substance was heated on a steam-bath with 0.6 g. of potassium hydroxide in 25 ml. of water. The solid gradually dissolved with a transitory dark red coloration. On cooling, 0.1 g. (9.5%) of N-phenyl-N'-(α-pyridyl)-urea was obtained; m.p. 184–185°. On admixture with an authentic sample (m.p. 187–189°), a melting point of 186–187.2° was observed.

Methyl N-(α-Pyridyl)-mesoxalamate *p*-Carbomethoxyphenylhydrazone.—When boiled with dilute aqueous sodium hydroxide, until the original red color of the solution had faded to a light yellow, cyanide ion was formed from this material, as indicated by the above test.

Ethyl N-(α-Pyridyl)-isonitrosomalonamate.—This compound was dissolved in excess 2% sodium hydroxide solution and allowed to stand for two days. The colorless solution gave a strong test for cyanide ion.

Ethyl N-(γ-Pyridyl)-mesoxalamate Phenylhydrazone.—This substance, which could not be hydrolyzed by aqueous base to produce cyanide, was prepared as follows.

Ethyl malonyl chloride was synthesized by the action of thionyl chloride on potassium ethyl malonate,[15] by the method of Staudinger,[16] in 40% yield; b.p. 60° (7 mm.) (reported[16] b.p. 63–64° (10 mm.)).

Ethyl N-(γ-Pyridyl)-malonamate Hydrochloride.—A solution of 7.8 g. (0.052 mole) of the acid chloride in 50 ml. of absolute ether was added to a mixture of 4.9 g. (0.052 mole) of γ-aminopyridine and 750 ml. of absolute ether. A white granular precipitate formed at once. The reaction mixture was allowed to stand overnight; the crude hydrochloride was filtered and dried in a desiccator to yield 9.5 g. (75%) of crude product.

Diazonium Coupling.—The crude hydrochloride (2.24 g., 0.01 mole) was added to a mixture of 5.6 g. of absolute alcohol, 11 g. of 50% aqueous alcohol, 1.1 g. of sodium acetate, and 0.53 g. (0.005 mole) of sodium carbonate. To this mixture was added dropwise a solution of 0.01 mole of benzenediazonium chloride, prepared from 0.93 g. of aniline, 5 ml. of water, 2 ml. of concentrated hydrochloric acid and 0.69 g. of sodium nitrite in 2 ml. of water. The product appeared as a red oil; it was extracted into chloroform, which was then allowed to evaporate in the air. Trituration of the resulting red oil with a small quantity of acetone

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(11) K. Feist, *Arch. Pharm.*, **272**, 100 (1934).

(12) The dipyridylurea was prepared by the method of R. Camps, *Arch. Pharm.*, **240**, 351 (1902); m.p 174.5–176° (reported m.p. 175°).

(13) It may be noted that on acidification of a portion of this mixture, a heavy, intractable, base-soluble precipitate, presumably *p*-carboxyphenyl-α-pyridylurea, was formed. After several unsuccessful attempts at its purification, it was not examined further.

(14) A. E. Chichibabin and J. G. Bylinkin, *Ber.*, **55**, 998 (1922).

(15) W. J. Hickinbottom, "Reactions of Organic Compounds," Longmans Green and Co., London, 1948, p. 265.

(16) H. Staudinger and H. Becker, *Ber.*, **50**, 1019 (1917).

produced a yellow solid, which, after several recrystallizations from cyclohexane, melted at 144.5–145°.

Anal. Calcd. for $C_{16}H_{16}N_4O_3$: C, 61.38; H, 5.15; N, 17.90. Found: C, 61.58; H, 5.42; N, 18.03.

III. Reaction of IIa with Sodium Methoxide in Moist Methanol

In this reaction a sample of the product IIa which had been extracted with boiling isopropyl alcohol was employed. This material (5.32 g., 0.02 mole) was added to a solution of 0.04 mole of sodium methoxide in 100 ml. of ordinary methanol.[17] The mixture turned dark red, and after it had been refluxed for 9.5 hours all of the coupling product had dissolved. The solution was cooled and filtered from a tan solid (0.75 g.) which was found to be **sodium carbonate.** The solid was dissolved in a little hot water and filtered. To the cooled filtrate was added three parts of methanol; this caused the precipitation of a white solid, which was washed several times with hot methanol. An attempted ignition test showed it to be entirely inorganic. The gas evolved on treatment of the material with hydrochloric acid reacted with barium hydroxide solution to produce a white precipitate, which was soluble in hydrochloric acid with ebullition. On the basis of anhydrous sodium carbonate, the 0.75 g. of crude salt obtained from the reaction mixture represents 0.007 mole, or a 35% yield if one mole of carbon dioxide were formed from each mole of coupling product. In another run on a 0.01 molar scale, a 10.5-hour reflux period produced 0.59 g. (56%) of the salt.

The filtrate from the sodium carbonate, which had a strong hydrogen cyanide odor and gave a strong prussian blue test, was evaporated in an air stream at room temperature, and the resulting brown solid was extracted with three 150-ml. portions of water; the water-insoluble residue (1.58 g.) was set aside (see below). To the water extracts glacial acetic acid was added to *p*H 5 to precipitate 1.39 g. of a yellow solid, which was collected and dried. Extraction of this material with hot cyclohexane permitted the separation of a light yellow solid from a small brown amorphous residue. Recrystallization of the yellow compound from the same solvent produced fine yellow filaments, which melted at 145–145.2° with decomposition, and resolidified on cooling. The compound proved to be the **phenylhydrazone of N-(α-pyridyl)-mesoxalamic acid.** The 1.39 g. of crude material, calculated on this basis, corresponds to a 24.4% yield.

Anal. Calcd. for $C_{14}H_{12}N_4O_3$: C, 59.16; H, 4.26; N, 19.71. Found: C, 59.66; H, 4.44; N, 19.81.

The identity of the free acid was proved by its methylation, with diazomethane, to form a methyl ester, m.p. 163.2–163.8°, which did not depress the m.p. of authentic methyl N-(α-pyridyl)-mesoxalamate phenylhydrazone.[1]

After standing 12 hours in 2.5% sodium hydroxide the phenylhydrazone of N-(α-pyridyl)-mesoxalamic acid gave a strong prussian blue test.

The above acid, in a test-tube equipped with a connection to a vessel of barium hydroxide solution, was slowly heated on an oil-bath to its melting point. As the temperature was gradually raised, a white precipitate formed in the trap; ebullition was quite rapid at 120–130°. The white barium precipitate was soluble in hydrochloric acid with ebullition. The test-tube contained a reddish solid, which had a strong hydrogen cyanide odor, and the filtrate from the barium carbonate gave a strong positive test for the cyanide ion. Repeated recrystallization of the red solid from cyclohexane produced yellow filaments of nearly pure N-phenyl-N′-(α-pyridyl)-urea, m.p. 185°.

Anal. Calcd. for $C_{12}H_{11}N_3O$: C, 67.59; H, 5.20; N, 19.71. Found: C, 67.98; H, 5.30; N, 19.91.

When mixed with an authentic sample of the urea, m.p. 187–188°, this product melted at 186–187°.

The same compound was also produced inadvertently from the above acid at a lower temperature. In an attempt to improve the isolation of N-(α-pyridyl)-mesoxalamic acid phenylhydrazone, the crude acidification product was extracted overnight in a soxhlet extractor with cyclohexane. Instead of the expected acid, the crude urea, m.p. 181–183.5°, was found in the pot. On admixture with the above decarboxylation product (m.p. 185°) a mixed melting point of 182–184° was observed. It is therefore apparent that slow decarboxylation and loss of hydrogen cyanide take place even at the temperature of boiling cyclohexane.

The water-insoluble fraction (1.58 g.) of the material obtained by evaporation of the methanol solution (see above) was recrystallized from cyclohexane. From this solvent were obtained white, hair-like filaments of methyl N-(α-pyridyl)-carbamate, m.p. 128–129°.

Anal. Calcd. for $C_7H_8N_2O_2$: C, 55.25; H, 5.30; N, 18.42. Found: C, 54.93; H, 5.12; N, 18.63.

The 1.58 g. of compound obtained from this reaction is 0.0104 mole, 52%. In another run a 58% yield of the once-recrystallized urethan was obtained.

The ester was prepared independently by the addition of a solution of 9.45 g. (0.1 mole) of methyl chlorocarbonate in 95 ml. of absolute ether to a solution of 9.41 g. (0.1 mole) of α-aminopyridine in the same quantity of ether.[18] The mixture was allowed to stand for 10 minutes, then the yellow-white gummy solid which had formed was washed with 100 ml. of saturated aqueous sodium bicarbonate, the resulting liquid layers were separated, and the ether was dried and evaporated. White filaments (4.9 g., 32%) were obtained. After recrystallizations from cyclohexane and aqueous methanol they melted at 128.5–129.2°, and on admixture with the above sample obtained from the sodium methoxide reaction, melted at 128.5–129.5°.

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[17] If the methanol contained 0.50% of water by weight, slightly more than 0.02 mole of water was present.

[18] This preparation was patterned after that of R. Camps, reference 12, for the corresponding ethyl ester.