lized from hexane again. Yield 57.4 g. (34.6%); m.p. 147–148°.

Anal. Calcd. for $C_{12}H_{22}N_2S$: C, 63.66; H, 9.80; N, 12.38. Found: C, 63.76; H, 9.62; N, 12.60.

Picrate: Recrystallized from ethanol; m.p. 207–208°.

Anal. Calcd. for $C_{18}H_{25}N_5SO_7$: N, 15.38. Found: N, 15.71.

Benzamide: Recrystallized from ethanol-water; m.p. 86–87°.

Anal. Calcd. for $C_{19}H_{26}N_2SO$: N, 8.48. Found: N, 8.71.

3-Methylimino-4-nitroso-1,5,5-trimethyl-2-thia-4-azabicyclo-[4.2.2]decane (XI). A solution of 3 g. of X in 25 cc. glacial acetic acid was treated with excess cold 10% aqueous sodium nitrite. An oil formed after several minutes which solidified on standing in the cold overnight. The light yellow solid was collected on a suction filter and washed with cold water. Crystallization was accomplished by dissolving the compound in ethanol, warming the solution slightly, adding water to cloudiness, warming until solution occurs again, and allowing the solution to cool slowly in a stoppered test tube placed in water bath. Clear, cubic, faintly yellow crystals, m.p. 39–40°, were produced.

Anal. Calcd. for $C_{12}H_{21}N_3SO$: N, 16.45. Found: N, 16.81.

The compound gave a positive Liebermann's test and evolved nitrous acid when treated with concentrated hydrochloric acid.

3-Anilino-1,5,5-trimethyl-2-thia-4-azabicyclo[4.2.2]dec-3-ene (XIII). A mixture consisting of 50 g. (0.369 mole) +-limonene, 99 g. (0.65 mole) phenylthiourea, and 92.5 g. (0.485 mole) *p*-toluenesulfonic acid was heated and stirred on the steam bath for three days. The brown oily product was washed with ether and water and then warmed with excess 4*N* sodium hydroxide. The solid, which was produced, was separated and recrystallized from ethanol; yield 22 g. (20.6%), m.p. 165–166°.

Anal. Calcd. for $C_{17}H_{24}N_2S$: C, 70.78; H, 8.39; N, 9.71. Found: C, 70.70; H, 8.25; N, 9.93.

Picrate: Recrystallized from methyl ethyl ketone; m.p. 237–238°.

Anal. Calcd. for $C_{23}H_{27}N_5SO_7$: C, 53.37; H, 5.26; N, 13.53. Found: C, 54.38; H, 5.35; N, 14.00.

Benzamide: Recrystallized from hexane-cyclohexane; m.p. 140–141°.

Anal. Calcd. for $C_{24}H_{28}N_2SO$: C, 73.43; H, 7.19; N, 7.14. Found: C, 73.90; H, 6.98; N, 7.51.

3-Phenylimino-4-nitroso-1,5,5-trimethyl-2-thia-4-azabicyclo-[4.2.2.]decane (XIV). A solution of 5 g. in 25 cc. cold glacial acetic acid was treated with excess cold 10% aqueous sodium nitrite. A yellow oil precipitated which solidified on standing overnight. The solid was collected on a suction filter. Recrystallization from absolute ethanol yielded light yellow crystals; m.p. 115–116°.

Anal. Calcd. for $C_{17}H_{23}N_3SO$: N, 13.24. Found: N, 12.46.

EVANSTON, ILL.

[CONTRIBUTION FROM THE OHIO STATE UNIVERSITY RESEARCH FOUNDATION]

Products from Reaction of Hydrazine and Thionooxamic Acid and Their Conversion into Heterocyclic Compounds[1]

RUDI RÄTZ AND HANSJUERGEN SCHROEDER

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Contrary to literature statements free thionooxamic acid, $H_2N—CS—COOH$, could be isolated and was found to be absolutely stable in the solid state. This acid is highly reactive to hydrazine and yielded, depending on the amount of hydrazine, oxalamidrazone and oxalhydrazidine. Oxalamidrazone was used for the synthesis of new 1, 2, 4-triazinecarbonic esters.

Thionooxamic acid (I), $NH_2—C(=S)—COOH$, has been reported only in the form of its salts and derivatives, *e.g.* esters, amides, etc. All attempts to prepare the free acid from alkali salts, even under mild conditions, resulted in failure, since the aqueous solution of I, obtained by adding the required amount of dilute mineral acid to the aqueous solution of an alkali thiono-oxamate, undergoes rapid decomposition with separation of elemental sulfur. Therefore I was described as incapable of existence in the free state.[2]

We have found, however, that immediate extraction of the aqueous solution of I by certain organic solvents, such as diethyl ether or ethyl acetate, leads to stable yellow prismatic crystals of I, m.p. 113°. These crystals of I have been stored for over two years without signs of decomposition.

Due to the presence of a free carboxylic and a thioamide group in its molecule, I represents a highly reactive compound. In order to obtain components for the synthesis of *N*-heterocyclics, the reaction of I with hydrazine (II) was studied.

Depending on the conditions different reaction products may be obtained from I and II. In ethanolic solution I reacted with one mole of anhydrous II to give the hydrazinium thionooxamate (III) which reacted vigorously with cold water to hydrogen sulfide and oxamic acid hydrazone (IV) (oxalamidrazone). Upon heating at 200°, IV decomposed with loss of ammonia and carbon dioxide. The yet unknown formamidrazone (V) could not be isolated as an intermediate during this thermal reaction, since at least under these conditions immediate self-condensation with formation of 4-amino-1,2,4-triazole (VI) occurred. This reaction and earlier observations[3] indicate

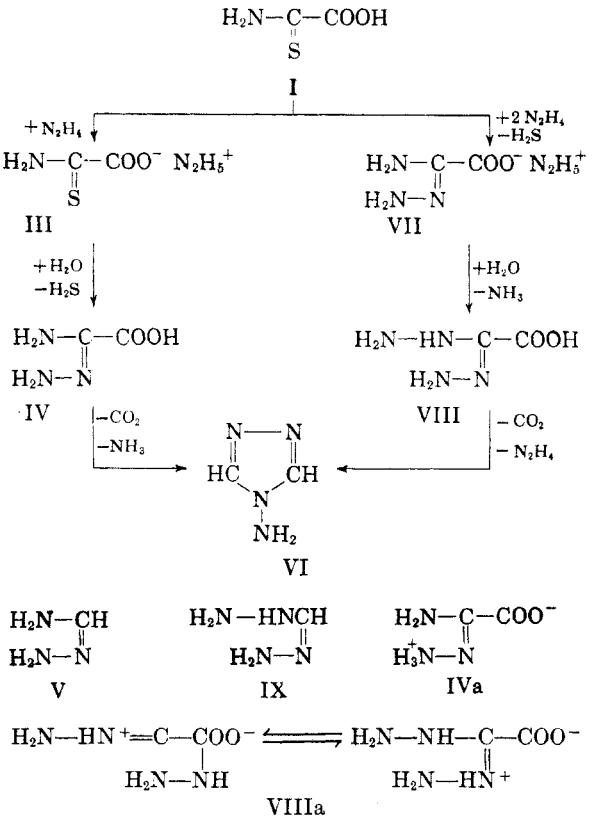
(1) This article is based on work performed under Project 116-B of The Ohio State University Research Foundation sponsored by the Olin Mathieson Chemical Corp., New York, N. Y.

(2) H. Weddige, *J. prakt. Chem.* (2), **9**, 137 (1874).

(3) Ch. Grundmann and R. Rätz, *J. Org. Chem.*, **21**, 1037 (1956).

that formamidrazone itself, if able to exist at all, probably is a very reactive and unstable compound.

If the acid I was allowed to react with two moles of anhydrous hydrazine in ethanolic solution, evolution of hydrogen sulfide occurred immediately and the hydrazinium salt of IV was formed (VII). This salt underwent an interesting rearrangement when treated with water, leading to the yellow oxalhydrazidine (oxalic acid hydrazide hydrazone) (VIII), one of the very few known true aliphatic



hydrazidines. Upon thermal treatment at 200° VIII decarboxylated with self-condensation, forming VI in a high yield. Also in this case, the possible first reaction product formhydrazidine (IX) could not be isolated.

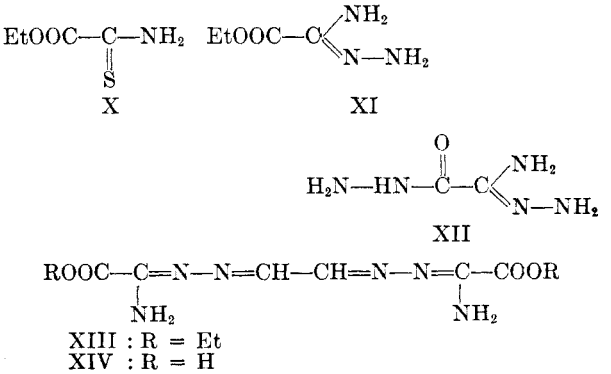
Free aliphatic hydrazidines, such as VIII, are not described in the literature. The few known representatives were always isolated in the form of their salts, *e.g.* with hydrochloric acid.[4] In the case of VIII the stability of the free hydrazidine might be due to an intramolecular salt formation. Therefore the character of VIII is better expressed by the betaine formula VIIIa. The same considerations are valid for IV and expressed by the formula IVa.

In accordance with the betaine structure, IV and VIII are insoluble in ether and ethanol. VIII can be recrystallized from water; IV from aqueous 50% ethanol. Also VIII was not soluble in cold 2*N* HCl, but upon heating at 90° decarboxylation and formation of II—HCl and HCOOH took place. In 10% aqueous ammonia VIII could be dissolved and reprecipitated unchanged at pH 9.5–10.0 by acid addition. The dilute aqueous solution of VIII gave precipitates with the salts of the alkaline earth and heavy metals, such as copper, silver, and lead.

When VIII was refluxed with 90% formic acid for 15 min. a quantitative yield of *N,N'*-diformylhydrazine, m.p. 162° was obtained. No ring-closure reaction was observed by allowing VIII to react with ethyl nitrite in methanolic hydrochloric acid.

The amidrazone IV and the corresponding ethyl ester, ethyl oxalamidrazonate (XI) were found to be interesting intermediates for the synthesis of 1,2,4-triazine derivatives.[5] The ester XI was not prepared from I or its hydrazine-reaction products, but by reaction of ethyl thiono-oxamate (X) with one mole of II. Neither amidrazone IV nor XI reacts with glyoxal with ring-closure to the desired *as*-triazine-3-carboxylic acid or the ethyl ester respectively, but to open chain derivatives (XIV and XIII) formed from two moles of IV and XI, respectively, and one mole of glyoxal. This behavior is strictly analogous to that of semicarbazide and aminoguanidine.[6] Since aminoguanidine in the form of its bicarbonate was recently used successfully in a ring closure reaction with glyoxal to form 1,2,4-triazine derivatives,[7] we expended much effort attempting the cyclization of IV and XI with glyoxal under a wide variety of conditions, but always the open-chain derivatives, XIV and XIII respectively, were formed.

Diethyl dioxosuccinate however, which may be considered as carbethoxylated glyoxal, condensed readily with X to give 3,5,6-triscarbethoxy-*as*-triazine (XV). The condensation of IV with diethyl dioxosuccinate resulted in the formation of 5,6-dicarbethoxy-*as*-triazine (XVI), ring closure and

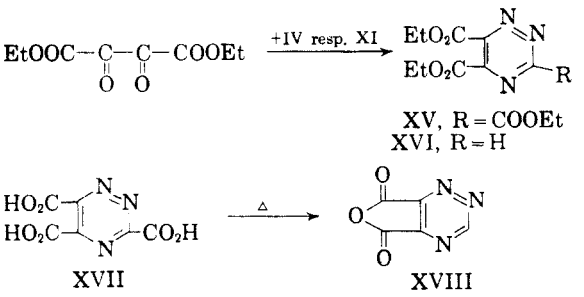


(4) W. Oberhummer, *Monatsh.*, **63**, 285 (1933).

(5) While this work was in progress, a publication of P. Schmidt and J. Druey, *Helv. Chim. Acta*, **38**, 1560 (1955), appeared which describes the preparation of X by essentially the same procedure and also some condensations of X with 1,2-dicarbonyl compounds to substituted *as*-triazines.

(6) J. Thiele and E. Dralk, *Ann.*, **302**, 275 (1898).

(7) J. G. Erickson, *J. Am. Chem. Soc.*, **74**, 4706 (1952).



XV, R = COOEt
XVI, R = H

XVII XVIII

decarboxylation at the 3-position occurring simultaneously.

The tricarboxylic ester XV could be converted *via* the potassium and lead salt into the *as*-triazine-3,5,6-tricarboxylic acid (XVII). In contrast to its isomer of the *s*-triazine series,[8] the triacid XVII did not yield any traces of the yet unknown parent compound *as*-triazine, when decarboxylation was attempted under a wide variety of conditions. The primary product of this reaction was the anhydride of *as*-triazine-5,6-dicarboxylic acid (XVIII) which could be isolated in several cases. It became obvious that no simple thermal reaction can further degrade XVIII to the desired *as*-triazine. An attempt to decarboxylate XVII with 5% aqueous hydrochloric acid at 220° in a sealed tube, a method sometimes successful in the heterocyclic series,[9] met with total degradation of the *as*-triazine ring. For these reasons, XVI did not offer any better chance than XV for the conversion into *as*-triazine.

EXPERIMENTAL[10]

Thiooxamic acid (I). Potassium thiooxamate (14.3 g., 0.1 mole) was dissolved in 100 ml. of *N* hydrochloric acid and the clear solution was immediately extracted with four 20-ml. portions of diethyl ether. The combined extracts were dried over sodium sulfate and after removal of the ether *in vacuo*, the residue was crystallized from chloroform to give I (8.27 g., 78%), yellow prisms, m.p. 113° (with decomposition).

Anal. Calcd. for $C_2H_3NO_2S$: C, 22.83; H, 2.85; N, 13.32; S, 30.42. Found: C, 22.93; H, 2.85; N, 13.28; S, 30.41.

Oxalamidrazone (IV). A solution of anhydrous hydrazine (3.2 g., 0.1 mole) in absolute ethanol (50 ml.) was added dropwise with stirring and ice cooling to a solution of I (10.5 g., 0.1 mole) in 100 ml. of absolute ethanol. The yellowish crystalline precipitate was filtered, washed twice with 50 ml. of absolute ethanol, and dried over phosphorus pentoxide. Yield: 9.83 g. of hydrazinium thionoamidooxalate (III).

When III (13.7 g., 0.1 mole) was dissolved in 40 ml. of cold water, a violent evolution of hydrogen sulfide began immediately. After 1 hr. ethanol was added until crystallization occurred. After standing overnight, the crystalline product was filtered and recrystallized from 70% aqueous ethanol to give IV, 8.95 g. (87%), fine white needles, decomposing at 194–196°.

Anal. Calcd. for $C_2H_5N_3O_2$: C, 23.26; H, 4.88; N, 40.69. Found: C, 23.42, 23.36; H, 5.21, 5.29; N, 40.44, 40.53.

Thermal decomposition of IV *to 4-amino-1,2,4-triazole* (VI). IV (5 g.) was heated in a distillation flask at 250°. The crystalline residue (1.9 g.) was taken up in ethanol, the solution filtered and ether added until turbidity occurred. After standing overnight at −20°, large crystals, m.p. 78–79°, were obtained and identified by a mixed melting point with an authentic sample of VI.

Anal. Calcd. for $C_2H_4N_4$: C, 28.57; H, 4.80; N, 66.64. Found: C, 28.36; H, 4.86; N, 66.41.

Oxalhydrazidine (VIII). A solution of anhydrous hydrazine (6.4 g., 0.2 mole) in absolute ethanol (50 ml.) was added dropwise with stirring and ice cooling to a solution of I (10.5 g., 0.1 mole) in 100 ml. of absolute ethanol. After 2 hr. the yellowish crystalline precipitate of the hydrazinium salt VII (10.5 g.) was filtered, washed twice with 50-ml. portions of ethanol and dried over phosphorus pentoxide.

VII (13.5 g., 0.1 mole) was dissolved in 100 ml. of hot water. After cooling to room temperature, filtration gave VIII (11 g., 95%), yellow needles, m.p. 197°. Several recrystallizations from water raised the melting point to 208–209°, but the yellow color of the crystals could not be removed, even with the addition of charcoal.

Anal. Calcd. for $C_2H_6O_2N_4$: C, 20.34; H, 5.12; N, 47.44. Found: C, 20.66; H, 5.12; N, 47.59.

VIII is insoluble in ether and ethanol, but soluble in 10% aqueous ammonia. It can be reprecipitated by adding HCl up to *p*H 9.5. The following ions gave amorphous precipitations: Ba^{++}, Ag^{+}, Pb^{++}, Cu^{++}.

When VIII was decomposed thermally in the same manner as described above for oxalamidrazone, *4-amino-1,2,4-triazole* (VI), m.p. 80–81°, was produced in good yield. VI was identified by mixed melting point with an authentic sample.

Boiling VIII with formic acid did not give the expected tetrazine derivative, but resulted in the degradation of VIII and formation of *N,N'-diformylhydrazine*, m.p. 162°.

Anal. Calcd. for $C_2H_4N_2O_2$: C, 27.21; H, 4.60; N, 31.80. Found: C, 27.31; H, 4.56; N, 31.82.

Ethyl oxamidrazonate (XI). A solution of hydrazine hydrate (10.0 g., 0.2 mole) in ethanol (100 ml.) was added dropwise with stirring to a solution of ethyl thionoamidooxalate[11] (X, 26.6 g., 0.2 mole) in 600 ml. of ethanol and the mixture was stirred for 3 hr. After standing overnight, the ethanol was evaporated in vacuo to give 25 g. of a reddish, crude product, from which pure XI was best obtained by repeated extraction (8–10 times) with a boiling mixture of 300 ml. of ligroin and 100 ml. of methylene chloride. On cooling the combined extracts gave 13 g. of XI, fine colorless needles, m.p. 96°, identical with the product described by Schmidt and Druey.[5]

Hydrazine hydrate (4.9 g., 0.1 mole) reacted with a solution of X (6.7 g., 0.05 mole) in 20 ml. of ethanol to give ethanol-insoluble *oxalamidrazone hydrazide* (XII) in quantitative yield. XII crystallized from 80% ethanol in small yellowish needles which turned orange and then red above 140°, and melted partially at 154°, but resolidified at 158°.

Anal. Calcd. for $C_2H_7N_5O$: C, 20.53; H, 6.03; N, 59.85. Found: C, 20.50; H, 5.86; N, 59.70.

Reaction of ethyl oxalamidrazonate (XI) *with glyoxal.* A solution of XI (2.6 g., 0.02 mole) in 2600 ml. of ethanol was added dropwise with stirring at room temperature over a period of 100 hr. to a solution of glyoxal (3.84 g., in form of a 30% aqueous solution) in 3800 ml. of ethanol. The yellow solution was then concentrated at 50° to a volume of 15 ml. The azine XIII (0.4 g.) separated in golden yellow rhombohedral crystals; m.p. 227°, after two recrystallizations from chloroform and sublimation at 200°/3 mm. Complete evaporation of the filtrate gave a highly viscous oil which solidified to a brown resin. No ether soluble material could be extracted from it.

(8) Ch. Grundmann and E. Kober, *J. Org. Chem.*, **21**, 1392 (1956).

(9) E. Tauber, *Ber.*, **28**, 453 (1895); R. Stoermer and O. Gaus, *Ber.*, **45**, 3112 (1912).

(10) All melting points are determined with the Fisher-Johns apparatus. Microanalyses are from Galbraith Laboratories, Knoxville, Tenn., and from Spang Microanalytical Laboratory, Ann Arbor, Mich.

(11) A. Reissert, *Ber.*, **37**, 3721 (1904).

When this condensation was run at higher concentrations, the yield of XIII was considerably higher and the resin yield lower. For example, a solution of 0.515 g. of XI in 10 ml. of ethanol added dropwise with stirring to a solution of 0.74 g. of glyoxal (as a 30% aqueous solution) in 5 ml. of ethanol yielded 0.3 g. of XIII.

Anal. Calcd. for $C_{10}H_{16}N_6O_4$: C, 42.25; H, 5.64; N, 29.55. Found: C, 42.24; H, 5.75; N, 29.54.

Hydrolysis of XIII with ethanolic potassium hydroxide gave the dipotassium salt as small yellowish needles from 40% aqueous ethanol, m.p. 307° (dec.).

Anal. Calcd. for $C_6H_6N_6O_4K_2$: C, 23.63; H, 1.98; N, 27.61; K, 26.65. Found: C, 23.05; H, 1.99; N, 28.23; K, 26.05.

Addition of HCl to an aqueous solution of the above potassium salt gave a slightly yellowish precipitate of the free acid (XIV), m.p. 165° (dec.) after one recrystallization from a large amount of water.

Anal. Calcd. for $C_6H_8N_6O_4 \cdot 2\ H_2O$: C, 27.22; H, 4.88; N, 31.88. Found: C, 27.70; H, 4.63; N, 31.78.

Reaction of oxalamidrazone (IV) *with glyoxal.* To a solution of glyoxal (7.7 g. in form of a 30% aqueous solution) in 70 ml. of ethanol was added a suspension of IV (4.1 g.) in 100 ml. of ethanol at room temperature with stirring over a period of 30 min. From the almost clear solution slightly yellowish crystals of XIV (4 g.) separated on standing overnight. The material, thus obtained, was identical with the acid obtained above by saponification of the diethylester XIII. M.p. 163–164° (dec.).

3,5,6-Triscarbethoxy-as-triazine (XV). To a solution of diethyl dioxosuccinate (37.4 g.) in ethanol (140 ml.) a solution of XI (24.2 g.) in 470 ml. of ethanol was added dropwise in 1 hr. at room temperature with stirring. The solution became deep yellow upon the addition of the amidrazone. After standing overnight, the mixture was refluxed for 2 hr. and the ethanol removed by vacuum distillation. To the brown oily residue was added 200 ml. of ether whereupon semi-solid by-products separated. After filtration the ether was removed *in vacuo* and the residue distilled at 5 mm. The crude ester (38 g.) was dissolved again in 200 ml. of diethyl ether and the ethereal solution washed twice with 10-ml. portions of 2*N* HCl, twice with 10-ml. portions of saturated $NaHCO_3$ solution, and finally with water. After drying over sodium sulfate, the filtered solution was evaporated under reduced pressure and the oily residue redistilled to give XV, a dense orange-yellow oil with no tendency for crystallization at −15°, b.p.$_1$: 168–169°, b.p.$_3$: 173°, $n_D^{26°}$: 1.4949, yield: 40%.

Anal. Calcd. for $C_{12}H_{15}O_6N_3$: C, 48.48; H, 5.09; N, 14.14. Found: C, 48.61, 48.50; H, 4.98, 5.19; N, 14.04, 14.10.

as-Triazine-3,5,6-tricarboxylic acid (XVII). A solution of potassium hydroxide (16.4 g.) in 400 ml. of ethanol was added dropwise with shaking and ice cooling to a solution of the ester XV (22.1 g., 0.075 mole) in 50 ml. of ethanol. After standing overnight, the yellowish microcrystalline salt (24.1 g., 100%) was filtered and washed several times with ethanol. The salt crystallized from 50% aqueous ethanol in fine yellowish needles which did not melt below 300°.

Anal. Calcd. for $C_6K_3N_3O_6 \cdot H_2O$: C, 20.86; H, 0.58; K, 33.96; N, 12.17. Found: C, 20.38; H, 1.12; K, 33.75; N, 12.41.

The aqueous solution of the potassium salt gave an immediate yellowish precipitate with Ag^+ and Pb^{++}, and with Cu^{++} a green-blue precipitate appeared on standing overnight. No precipitation occurred on addition of alkaline earth metal ions.

A solution of the tripotassium salt of XVII (6.54 g.) in 40 ml. of water was added slowly with shaking to the solution of lead acetate (17.4 g., 50% excess) in 100 ml. of water. The precipitate was filtered and, for purification, twice suspended in 100 ml. of water and refiltered. The wet lead salt was suspended in 200 ml. of distilled water and treated with a stream of hydrogen sulfide for 1 hr. with stirring. After 2 hr., the lead sulfide was filtered and washed thoroughly with warm water (120 ml.) to extract remaining acid. The combined filtrates were evaporated at room temperature to dryness. For complete purification the crude acid (3.18 g., 76.5%) was retransformed into the lead salt. Liberation of the acid from the now practically alkali-free lead salt by means of hydrogen sulfide and drying of this acid over phosphorus pentoxide at room temperature for 10 days gave an anhydrous product.

Anal. Calcd. for $C_6H_3N_3O_6$: C, 33.81; H, 1.42; N, 19.72. Found. C, 33.84; H, 1.62; N, 19.59.

Attempts to decarboxylate XVII under various conditions met with failure. Around 170° the acid started to decompose to give a voluminous dark solid resin. The few droplets of distillate obtained contained only water and ammonia. The latter was identified as picrate and chloroplatinate. At still higher temperatures, a small amount of ammonium hydrogen carbonate sublimed. Addition of copper powder as a catalyst did not alter these results.

In refluxing 1-hexanol, XVII started to decarboxylate immediately, thereby changing to an insoluble brown powder, m.p. 175–183°, the anhydride of *as*-triazine-5,6-dicarboxylic acid (XVIII). No solvent could be found from which XVIII would crystallize unchanged.

Anal. Calcd. for $C_5HN_3O_3$: C, 37.90; H, 0.63; N, 26.50. Found: C, 37.26; H, 0.42; N, 27.80.

The hexanol filtrate of XVIII did not contain basic products.

Decarboxylation of XVII in boiling diphenyl ether yielded a yellow-brown solid product which changed within a very short period to a dark tarry product. No evidence for the formation of basic material was found.

The attempted decarboxylation to the parent compound in 5% HCl at 130° in a sealed tube also resulted in failure. No ethanol-soluble product was obtained from the residue after filtering the solution from carbonized particles and evaporating to dryness. Vacuum sublimation gave only ammonium chloride, indicating that a decomposition of the *as*-triazine ring had taken place during the treatment with HCl. The residue of the sublimation was a dark brown gummy material. No crystalline picrate or chloroplatinate could be obtained from its aqueous solution.

5,6-Dicarbethoxy-as-triazine (XVI). Carefully powdered IV (1.03 g., 0.01 mole) was added to a solution of diethyl dioxosuccinate (2.02 g., 0.01 mole) in absolute ethanol (50 ml.). The suspension was shaken for three days at room temperature—after two days most of the carboxy-formamidrazone had dissolved—the ethanol was evaporated *in vacuo* and the oily residue was dissolved in 100 ml. of diethyl ether. After filtration and removal of the solvent the residue was fractionated to give XVI (1.0 g., 44%), b.p. 165°/5 mm., $n_D^{29°}$ 1.4859, a yellow oil.

Anal. Calcd. for $C_9H_{11}N_3O_4$: C, 48.00; H, 4.92; N, 18.66. Found: C, 48.06; H, 4.85; N, 18.69.

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COLUMBUS, OHIO