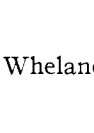
the very similar reactivities of the two substrates. The acid ionization constants (K_2) are reported to be 10^{-14} and $10^{-14.5}$ for Py and Im, respectively,[16] indicating that the equilibrium concentrations of anions available for iodination is of the same order of magnitude for Py and Im in solutions of the same stoichiometric concentration. The other two factors, k_1/k_{-1} and k_3, cannot be separated. However, we note that the ratio k_1/k_{-1} will determine the steady-state concentration of the Wheland intermediate (); the formation of this intermediate involves localization of two electrons to form a σ-bond between C and I. Therefore, the atom localization energy at the 4-position of Py and Im should provide at least a semiquantitative comparison of the relative values of k_1/k_{-1} for the two substrates.

Brown[10] calculated atom localization energies for the 4-positions of Py and Im by the simple molecular orbital method (neglecting overlap) and made no distinction between the pyridine-type nitrogen (>N:) and the pyrrole-type nitrogen (N–H); that is, he assigned a common inductive parameter h for the coulomb integral $\alpha_N = \alpha_C + h\beta$ for the two N atoms. Here α_N is the coulomb integral for nitrogen, α_C that for carbon, and β is the resonance integral. Brown gave localization energies for values of h ranging from -1 to $+1$. Hamano and Hameka[17] calculated accurate dipole moments for Py and Im by a simple molecular orbital method, using $h = 2.70$ for the pyrrole-type N and $h = 0.38$ for the pyridine-type N. In the anion, both nitrogen atoms are pyridine types; hence a common h-value is applicable. Because of the accuracy of the Hamano and Hameka calculations for the *molecules* of Py and Im, we assume $h = 0.38$ for the two pyridine-type atoms of the anion. Brown's atom localization energies for $h = 0.38$ are 2.1 ($-\beta$) for imidazole and 2.13 ($-\beta$) for pyrazole. If we assume that the entropies of formation of the Wheland intermediate for imidazole and pyrazole are comparable in magnitude, then these nearly identical atom localization energies suggest that the free energy of formation of the intermediates of Py and Im will likewise be comparable, and therefore that k_1/k_{-1} of the two substrates will have nearly the same value. We may conclude therefore that the rate-determining rate constants (k_3) of Py and Im must also have nearly the same value. The comparable values of the experimental activation energies of the "uncatalyzed" reactions of Py and Im support this argument, since any significant difference in the energy barriers of the rate-determining reactions would be reflected by a difference in the experimental activation energies.[18]

Acknowledgment.—We wish to thank Dr. D. E. Boswell of Socony–Mobile Oil Co., Inc., for helpful suggestions.

(16) A. Albert, "Heterocyclic Chemistry," Essential Books, Fair Lawn, N. J., 1959, p. 143.

(17) H. Hamano and H. F. Hameka, *Tetrahedron*, **18**, 985 (1962).

(18) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 209 ff.

[JOINT CONTRIBUTION FROM THE ELECTROCHEMICALS DEPARTMENT AND THE CENTRAL RESEARCH DEPARTMENT, E. I. DU PONT DE NEMOURS AND CO., INC., WILMINGTON 98, DEL.]

Hydroxy-1,2,5-thiadiazoles. I. A Novel Route from Potassium Cyanide and Sulfur Dioxide

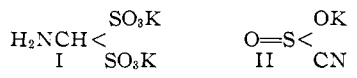
BY JOHN M. ROSS[1] AND WILLIAM C. SMITH[2]

RECEIVED OCTOBER 7, 1963

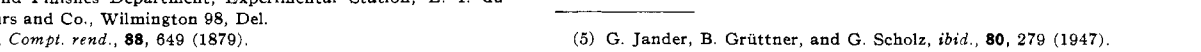
3-Cyano-4-hydroxy-1,2,5-thiadiazole has been obtained from the reaction of potassium cyanide and sulfur dioxide at 25–85° in the absence of hydroxylic solvents. The structure was elucidated by degradation to diethylaminoacetamide and to N-sulfamoyloxamic acid dipotassium salt, and by independent synthesis from isonitrosocyanoacetamide and sulfur dichloride. Various 3-hydroxy-1,2,5-thiadiazole derivatives were prepared including several potassium acid salts involving symmetrical hydrogen bonding of the acidic 3-hydroxyl proton.

The reaction of potassium cyanide and sulfur dioxide in aqueous solution has been known since Etard[3] obtained a crystalline product by passing sulfur dioxide through 40% aqueous potassium cyanide. The identity of this product as dipotassium aminomethanedisulfonate (I) was more clearly elucidated by von Pechmann and Manck.[4]

Reactions under other conditions have received only cursory examination. The formation of potassium cyanosulfinate (II) was postulated by Jander and co-workers[5] to account for the break in the potentiometric titration of potassium cyanide with sulfur dioxide dissolved in liquid hydrogen cyanide, but no reaction product was characterized.



More recently Seel and Müller[6] reinvestigated the work of Jander and co-workers and showed that the precipitate formed by addition of sulfur dioxide to a solution of potassium cyanide in liquid hydrogen cyanide was potassium pyrosulfite. They further studied the product obtained by prolonged exposure of potassium cyanide to liquid sulfur dioxide at room temperature and concluded that the over-all reaction could be described by the equation



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(2) Fabrics and Finishes Department, Experimental Station, E. I. du Pont de Nemours and Co., Wilmington 98, Del.

(3) A. Etard, *Compt. rend.*, **88**, 649 (1879).

(4) H. von Pechmann and Ph. Manck, *Ber.*, **28**, 2374 (1895).

(5) G. Jander, B. Grüttner, and G. Scholz, *ibid.*, **80**, 279 (1947).

(6) F. Seel and E. Müller, *ibid.*, **88**, 1747 (1955).

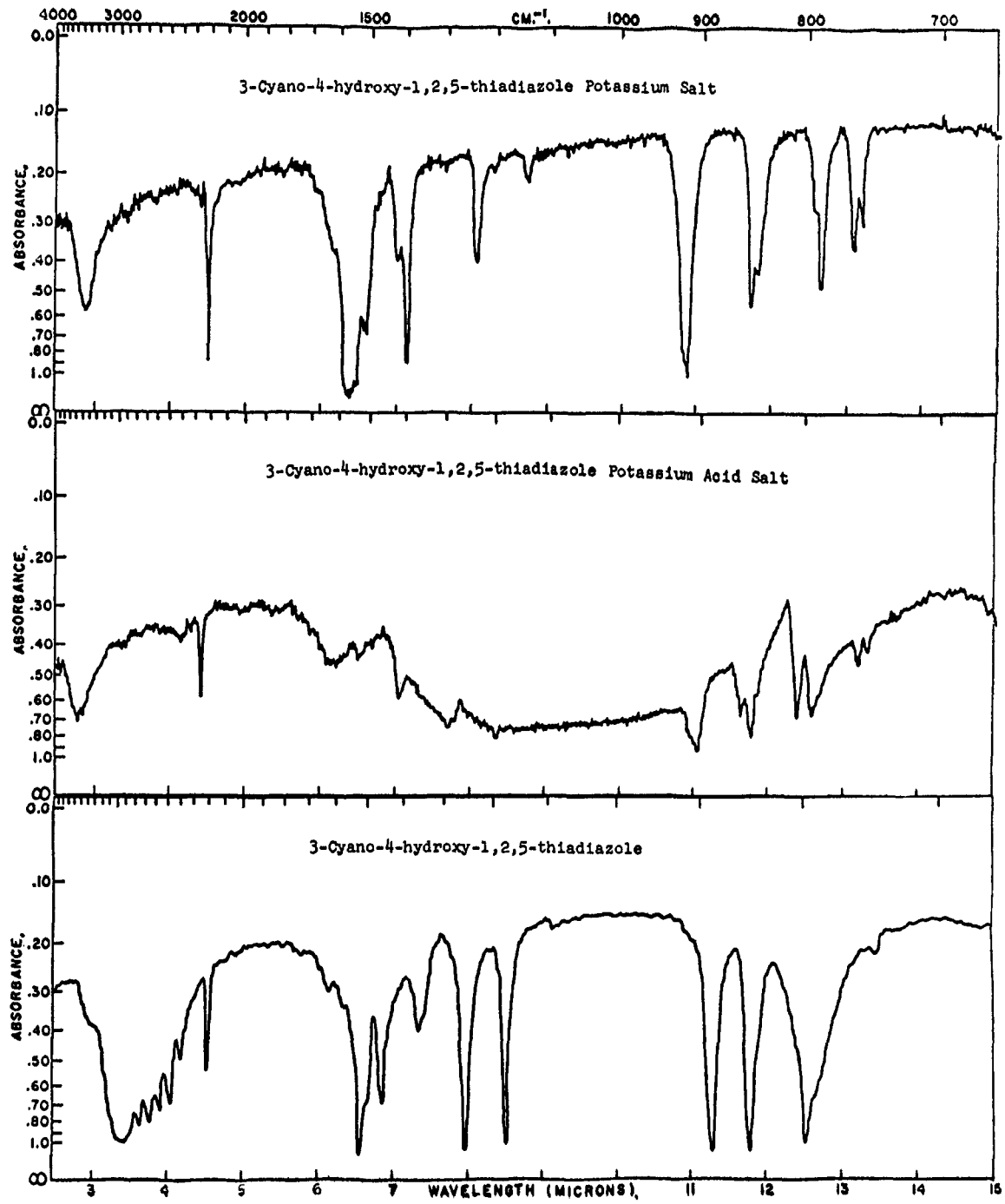
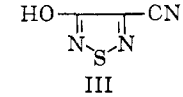


Fig. 1.—Infrared absorption spectra of 3-cyano-4-hydroxy-1,2,5-thiadiazole and salts determined as KBr pellets with a Perkin–Elmer Infracord recording spectrophotometer.

The present study as described herein was concerned with a study of this reaction system under nonaqueous conditions. It was undertaken after preliminary work showed that potassium cyanide and sulfur dioxide react readily and completely in the absence of a third component at moderate temperatures under autogenous pressure. Examination of the reaction product showed that a surprisingly high percentage of the resulting solid was soluble in a number of organic solvents, and far more than was anticipated from the product composition described by Seel and Müller. The solvent-insoluble residue was identified by X-ray diffraction and infrared analysis as predominantly potassium pyrosulfite.

Extraction of the crude solid product with dry acetonitrile, various aliphatic alcohols, or acetone removed up to 26 wt. % of a pale yellow crystalline solid which has been identified as the potassium salt of 3-cyano-4-hydroxy-1,2,5-thiadiazole (III). The characterization and chemistry of this compound are reported in this paper.

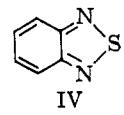


III

The particular monocyclic 1,2,5-thiadiazole ring system formed in this unusual inorganic reaction was first described in 1957, although the related 2,1,3-benzothiadiazole (IV) bicyclic systems have been known since the last century.[7] Most commonly,

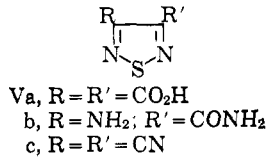
(7) O. Hinsberg, *Ber.*, **22**, 2895 (1889).

the monocyclic system IV has been obtained by

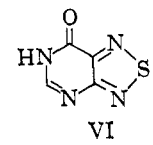


IV

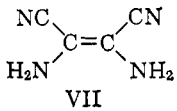
degradation of bicyclic systems and especially by oxidation of 2,1,3-benzothiadiazole derivatives[8-10] to 1,2,5-thiadiazole-3,4-dicarboxylic acid (Va) and very recently by basic cleavage of 1,2,5-thiadiazolo[3,4-*d*]-pyrimidine-7(6H)one (VI) to 4-amino-1,2,5-thiadiazole-3-carboxamide (Vb).[11] Two other interesting approaches explored at Indiana University by M. Carmack and associates have led to (a) a synthesis of 3,4-dicyano-1,2,5-thiadiazole (Vc)[12] based on the reaction of thionyl chloride and hydrogen cyanide tetramer (diaminomaleonitrile, VII), and (b) a general synthesis from substituted oxalimidates (VIII).[13]



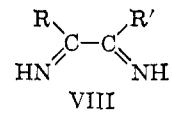
Va, R = R′ = CO_2H
b, R = NH_2; R′ = $CONH_2$
c, R = R′ = CN



VI



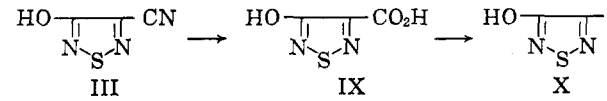
VII



VIII

3-Cyano-4-hydroxy-1,2,5-thiadiazole (III) itself may be isolated in almost quantitative yield from acidified aqueous solutions of both the potassium and potassium acid salts. This compound is a pale yellow, crystalline solid that melts at 160–162° and immediately resolidifies to a stable trimer which does not melt below 360°. The infrared spectrum (Fig. 1) has a strong nitrile band at 4.47 μ characteristic of a conjugated, unsaturated nitrile, together with a series of strong, sharp bands in the 3.0 to 4.2 μ region indicative of strong hydroxy hydrogen bonding. Elemental analyses and mass spectrometric analysis are also in accord with theory for this compound.

The presence of an acidic hydroxyl group, pK_a = 2.97, was confirmed by titration, salt formation, methylation, and proton magnetic resonance studies. This information (in combination with acid and alkaline hydrolysis studies which indicated the presence of only one nitrile group) led to the partial formula $C_2N_2S(OH)CN$, strongly indicative of a cyanohydroxythiadiazole. Drastic hydrolysis with 48% hydrobromic acid gave a yield of ammonium bromide sufficient to account for all three nitrogen atoms. Additionally, the inability to form hydrazine derivatives under such hydrolysis conditions indicated that the ring system was not a 1,2,3- or 1,3,4-thiadiazole. Further structural elucidation was simplified by elimination of the nitrile group by hydrolysis to the hydroxycarboxylic acid IX followed by decarboxylation to the hydroxythiadiazole X in a suitable high-boiling inert solvent.



III IX X

The possibility that the product was 5-hydroxy-1,2,4-thiadiazole was eliminated by direct comparison with an authentic sample kindly provided by Professor J. Goerdeler.[14]

The possible structures were thus narrowed down to 3-hydroxy-1,2,4-thiadiazole and 3-hydroxy-1,2,5-thiadiazole. Reductive desulfurization of the hydroxythiadiazole offered a promising route for distinguishing between these two possible structures, which theoretically would be expected to yield N-methylurea and glycinamide, respectively. Clemmensen reduction with zinc dust and ethanolic hydrogen chloride, which has been used successfully in the 1,2,4-thiadiazole series,[15] gave only an intractable gum. Reductive desulfurization with Raney nickel in 90% ethanol yielded a mixture of oil and crystals. The solid desulfurization product separated from *n*-hexane as colorless needles, m.p. 75.5–76.5°, of empirical formula $C_6H_{14}N_2O$ and was identified as N,N-diethylaminoacetamide.[16] This result led to the conclusion that the thiadiazole has structure X and that the potassium cyanide–sulfur dioxide reaction product must be 3-cyano-4-hydroxy-1,2,5-thiadiazole.

Additional confirmation of the 1,2,5-thiadiazole ring structure was obtained by aqueous permanganate oxidation of the hydroxythiadiazole X. Careful control of reaction conditions was necessary; vigorous oxidation gave only oxalic acid and potassium sulfate. Under milder conditions in aqueous solution at about 50° two products were obtained from separate experiments. A good yield of colorless crystals of sulfamoyloxamic acid dipotassium salt (XI) was isolated on one occasion and characterized by elemental analysis and infrared comparison with a sample[18] obtained by a similar permanganate oxidation of 1,2,5-thiadiazole-3,4-dicarboxylic acid. The product from another permanganate oxidation of the hydroxythiadiazole X was tentatively assigned the structure of 3,4-dihydroxy-1,2,5-thiadiazole 1,1-dioxide (XII) isolated as its monopotassium salt. This assignment is based on elemental analyses and the infrared spectrum which shows typical

(8) (a) A. M. Khaletskii, V. G. Pesin, and T. Chzhou, *Proc. Acad. Sci. U.S.S.R., Chem. Sect.* (English Transl.) **114**, 593 (1957); (b) V. G. Pesin, A. M. Khaletskii, and T. Chzhou, *J. Gen. Chem. U.S.S.R.*, **28**, 2126 (1958); (c) V. G. Pesin, A. M. Khaletskii, and E. K. D'yachenko, *ibid.*, **32**, 3440 (1962).

(9) (a) M. Carmack, L. M. Weinstock, and D. Shew, Abstracts, 136th National Meeting of the American Chemical Society, Sept., 1959, p. 37P; (b) E. M. Weinstock, *Dissertation Abstr.*, **19**, 3136 (1959); (c) U. S. Patents 2,980,687, 2,990,408, and 2,990,409 (1961).

(10) I. Sekikawa, *Bull. Chem. Soc. Japan*, **33**, 1229 (1960).

(11) Y. F. Shealy and J. D. Clayton, *J. Org. Chem.*, **28**, 1491 (1963).

(12) D. Shew, *Dissertation Abstr.*, **20**, 1593 (1959).

(13) R. Y. Wen, *ibid.*, **23**, 4121 (1963).

(14) J. Goerdeler, J. Ohm, and O. Tegtmeyer, *Ber.*, **89**, 1534 (1956).

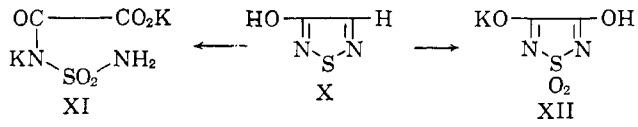
(15) A. W. Hofmann and S. Gabriel, *ibid.*, **25**, 1578 (1892); S. Ishikawa, *Chem. Zentr.*, **96** [2], 2206 (1925); F. Kurzer, *J. Chem. Soc.*, 2345 (1956).

(16) (a) The empirical formula of this unexpected product suggested that the compound was derived from interaction of the solvent with some intermediate reduction product. Examples of N-alkylations occurring during reactions with Raney nickel in aliphatic alcohols are known [R. Mozingo, D. E. Wolf, S. A. Harris, and K. Folkers, *J. Am. Chem. Soc.*, **65**, 1013 (1943); R. G. Rice and E. J. Kohn, *ibid.*, **77**, 4052 (1955); M. V. Rubtsov and E. S. Nikitskaya, *J. Appl. Chem. U.S.S.R.*, **29**, 2033 (1956)] and this possibility was checked by treating N-methylurea and glycinamide, respectively, with Raney nickel in boiling ethanol. The former was recovered unchanged. However, glycinamide was converted into the same mixture of oil and crystals obtained from the hydroxythiadiazole. The identity of the crystalline component as diethylaminoacetamide was confirmed by mixture melting point and infrared comparison with an authentic sample prepared by hydrolysis of diethylaminoacetonitrile.[17]

(17) T. W. Greenlee and W. A. Bonner, *J. Am. Chem. Soc.*, **81**, 4303 (1959), explain the formation of such N,N-dialkyl derivatives by reduction of Schiff bases formed by reaction of the amine with traces of aldehyde present in equilibrium with the alcohol in the presence of Raney nickel.

(18) This sample was generously donated by Professor M. Carmack.

sulfone absorption[19] at 7.40, 7.65, and 8.65 μ. Such a structure is a logical oxidation intermediate in the oxidation of X to XI. Also, previously reported 1,2,5-thiadiazole oxidation studies have shown that 1,1-dioxides can form[8] and that hydroxylation at a nuclear carbon atom can occur.[12]

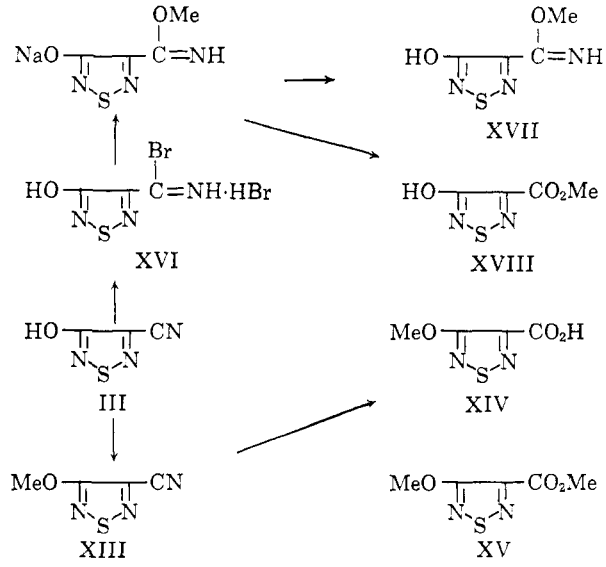


XI X XII

Further proof of structure III was achieved by independent synthesis under somewhat unexpected conditions, *i.e.*, by treating isonitrosocyanoacetamide with sulfur dichloride. Presumably an oxidative cyclization occurs with elimination of hydrogen chloride and hypochlorous acid (not isolated) resulting in good yields of 3-cyano-4-hydroxy-1,2,5-thiadiazole. Attempts to synthesize 3-hydroxy-1,2,5-thiadiazole-4-carboxamide by the reaction of iminomalonamide with sulfur dichloride or thionyl chloride were unsuccessful.

Reactions and Properties of 3-Hydroxy-1,2,5-thiadiazoles.—The 3-hydroxyl group of 1,2,5-thiadiazoles is remarkably acidic, and especially in the cyanohydroxy compound where the nitrile group exerts a strongly negative inductive effect. Salt formation is possible by direct displacement of weak acid salts such as carbonate, cyanide, and acetate. A large variety of salts was prepared, of which only the pale yellow silver salt is water insoluble. The acidity of the hydroxyl group prevented ester formation, and no reaction was observed with acetic anhydride, benzoyl chloride, or toluene-*p*-sulfonyl chloride. Alkylation of the hydroxyl group did not occur on treatment of the potassium salt with methyl iodide, but was achieved *via* the silver salt and more readily by methylation with diazomethane giving the methyl ether XIII. Saponification of XIII gave the methoxythiadiazolecarboxylic acid (XIV). The methoxycarboxylic methyl ester XV was obtained directly by treatment of IX with diazomethane. Attempts to prepare the methyl ester of 3-hydroxy-1,2,5-thiadiazole-4-carboxylic acid by the Pinner method of imidate ester formation led to the bromoimidate hydrobromide XVI which gave the hydroxy amide on heating with ethanol and regenerated the hydroxy nitrile on treatment with water. The ester was best prepared by isolation of the chloroimidate hydrochloride and treatment with sodium methoxide followed by acid hydrolysis which yielded a mixture of the free imidate ester XVII and the carboxylic methyl ester XVIII.

Attempts to thiolate the cyanohydroxythiadiazole with phosphorus pentasulfide in acetonitrile were unsuccessful, the thiadiazole being recovered unchanged. Attempts at replacing the hydroxyl group by halogen using a variety of chlorinating agents were almost entirely unsuccessful. Low yields of 3-chloro-1,2,5-thiadiazole derivatives were obtained by chlorination with phosphorus oxychloride in the presence of dimethylformamide, as indicated by dye formation on coupling the crude reaction products with various reagents. The resistance to direct replacement of the 3-hydroxyl group by chlorine resembles that of the



XVII XVI XVIII III XIV XIII XV

similarly located 3-hydroxyl group of 1,2,4-thiadiazoles.[20] Attempted chlorination of the cyanohydroxythiadiazole III with phosphorus pentachloride led only to trimerization involving the nitrile group to yield tris(hydroxythiadiazolyl)-*s*-triazine.

Trimerization of the cyanohydroxythiadiazole is most easily effected by heating the compound above its melting point. On melting (at 160–162°), the acidity of the melt is sufficient to catalyze the trimerization, resulting in recrystallization of the melt to the highly insoluble and thermally stable triazine. The trimer is sparingly soluble in aqueous alkali, from which it separates on neutralization, and in cold concentrated sulfuric acid, from which it may be precipitated on dilution with water. The infrared spectrum exhibits bands characteristic of the 1,2,5-thiadiazole nucleus and the triazine nucleus.

Hydrolysis of III with 6 *N* hydrochloric acid yielded the hydroxythiadiazolecarboxamide, but the product was always contaminated with some hydroxycarboxylic acid and some unchanged nitrile. A more convenient preparation is by hydrolysis of III in ethanolic potash which leads to precipitation of a quantitative yield of the potassium salt of the hydroxy carboxamide.

Aqueous alkaline hydrolysis of the nitrile III gave, on ethereal extraction of the acidified product, 80% yields of the colorless hydroxythiadiazolecarboxylic acid (IX). It was observed that acidification of the saponification mixture with sulfuric acid led to precipitation of a yellow crystalline product, m.p. 230° dec., having a somewhat variable analysis but one roughly corresponding to a 1:1 mixture of the hydroxycarboxylic acid and a monopotassium salt. Acidification of this acid salt with hydrochloric acid and ethereal extraction yielded the normal hydroxycarboxylic acid. This behavior is somewhat analogous to the stability of isothiazole-4,5-dicarboxylic acid monosodium salt to sulfuric acid.[21] The hydroxycarboxylic acid IX sublimes unchanged when heated above its melting point *in vacuo* but readily decarboxylates on heating above its melting point in an inert solvent such as nitrobenzene. Use of tetralin (b.p. 207°) as a decarboxylating medium led to degradation of the thiadiazole

(19) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 1st Ed., Methuen, London, 1954, p. 297.

(20) F. Kurzer and J. A. Taylor, *J. Chem. Soc.*, 3234 (1960).

(21) A. Adams and R. Slack, *ibid.*, 3061 (1959).

nucleus, with evolution of hydrogen sulfide and dehydrogenation of part of the solvent to naphthalene.

3-Hydroxy-1,2,5-thiadiazoles exhibit lactam–lactim tautomerism between the hydroxyl proton and the adjacent nuclear nitrogen atom. The absence of any major carbonyl absorption in the infrared spectra as determined using Nujol mulls or potassium bromide wafers excludes tautomerism occurring in the solid state to any significant extent, but this was observed in solution by ultraviolet spectroscopy and proton resonance studies. The cyanohydroxythiadiazole gives an ultraviolet absorption spectrum in ethanol (297 mμ, shoulder at 342) which closely resembles that of the 3-methoxy-4-cyano compound (296 mμ) in water. However, in water the cyanohydroxythiadiazole shows pronounced absorption at longer wave lengths (334 mμ) which is also exhibited by its neutral potassium salt. Proton resonance studies on the cyanohydroxy compound in acetonitrile showed that a single peak at −4.05 p.p.m. with respect to the CH_3 of acetonitrile was present. At such low field this must indicate the occurrence of lactam–lactim tautomerism, and this is apparently favored by solvents of high dielectric constant.

The 1,2,5-thiadiazole nucleus appears to be thermally stable up to 360°; a number of derivatives such as 3,4-dicyanothiadiazole and the hydroxycarboxylic acid sublime below this temperature. On heating the potassium salt of III above its melting point (305°), the melt was stable until close to 400° when sulfur was expelled from the nucleus and cyanogen evolved. Traces of oxygen were generated also and the residue was identified as a mixture of potassium thiocyanate and potassium cyanide. Stability of the 1,2,5-thiadiazole nucleus to reducing agents is severely limited; ring cleavage was observed during reactions with zinc and hydrochloric acid, sodium in boiling ethanol, and with sodium borohydride. Ring cleavage also occurred on treatment of thiadiazole derivatives with aqueous potassium bisulfite; the resultant substituted aminomethanesulfonates will be the subject of the second paper in this series.[22]

During the course of this work several examples of bimolecular acid salt formation were observed. Traces of moisture present in the acetonitrile used for solvent extraction of the potassium cyanide–sulfur dioxide reaction product led to isolation of a well-defined equimolecular mixture of the cyanohydroxythiadiazole and its potassium salt. On several occasions treatment of aqueous solutions of 3-hydroxy-1,2,5-thiadiazole-4-carboxamide potassium salt with aqueous potassium bisulfite led to recovery of the thiadiazole as an acid salt,[22] and a less well-defined example seems probable on acidification of aqueous solutions to the hydroxythiadiazolecarboxylic acid dipotassium salt with excess sulfuric acid. An unrelated example of this phenomenon was observed during the preparation of isonitrosocyanoacetamide by treatment of cyanoacetamide with potassium nitrite in acetic acid.

The acid salt products were identified by elemental analysis and by conversion to their respective potassium salts. The acid salts were easy to characterize by the similarity of their properties; in each case the acid salt was far less water soluble than either of its individual components and also exhibited a wide plateau of high absorption in the infrared between 9 and 11 μ, a region of transparency in the free hydroxyl compounds and their potassium salts (Fig. 1). Similar anomalous infrared absorption spectra have been observed with acid salts of carboxylic acids, and are the subject of recent papers by Speakman and co-workers.[23]

It seems reasonable that the proton associated with a strongly acidic hydroxyl should be capable of symmetrically linking individual molecules by a hydrogen bond in a manner similar to that observed with carboxylic acids and other acidic compounds such as the alkali bifluorides. Further evidence for the existence of strong hydrogen bonding occurring in the acid salt of cyanohydroxythiadiazole was obtained from its proton magnetic resonance spectrum in acetonitrile. A single signal corresponding to rapid proton exchange occurred in the free 3-cyano-4-hydroxy-1,2,5-thiadiazole at −4.05 p.p.m. (60 Mc./sec.) with respect to acetonitrile, whereas the peak was reduced to even lower field at −5.1 p.p.m. in the case of the potassium acid salt, indicative of the occurrence of strong hydrogen bonding. The existence of similar acid salts of compounds containing acidic hydroxyl groups must be fairly widespread, and the paucity of literature references is surprising. Very similar spectral behavior involving intense widespread background absorption has been reported to occur with acetamide hemihydrochloride.[24]

Experimental

General Remarks on the Reaction of Potassium Cyanide and Sulfur Dioxide.—Complete reaction is dependent upon the potassium cyanide–sulfur dioxide ratio, the reaction temperature, and the duration of the reaction. Greater than equimolecular amounts of sulfur dioxide are required for complete reaction, and for convenience it is preferable to employ a 2:1 molecular ratio so that the product is obtained in a powdered form easily removable from the reactor. The reaction time decreases rapidly with increase in temperature, ranging from 100 hr. at room temperature to less than 1.5 hr. at 75° (see Table I). At higher temperatures a vigorous exothermic reaction occurs and low yields of thiadiazole are isolated from the resultant black glass.

TABLE I

KCN–SO_2 REACTION VARIABLES

Excess SO_2, %	Reaction temp., °C.	Reaction time, hr.	Weight increase of solid charge, %
50	−78	240	90
50	25	24	54
25	25	100	108
25	50	5	99
100	50	6	113
22	60	6	86
31[a]	60	6	100
100	60	4	124
37	75	1.5	100
100	75	1.5	107
25	100	[b]	...
25	75	1	...
	100	[c]	

[a] Stirred autoclave reaction in the presence of dry acetonitrile; an exotherm to 94° occurred before external heat was applied. [b] Reaction "flashed" from 87 to 241°. [c] Reaction "flashed" to 190° after 5 min. at 100°.

Reactions under autogenous pressure may be performed in the presence of a number of nonhydroxylic solvents or, more con-

(22) J. M. Ross, *J. Am. Chem. Soc.*, **86**, 2869 (1964).

(23) H. N. Shrivastava and J. C. Speakman, *J. Chem. Soc.*, 1151 (1961); J. C. Speakman and H. H. Mills, *ibid.*, 1164 (1961).

(24) A. Albert and R. M. Badger, *J. Chem. Phys.*, **29**, 1193 (1958).

veniently, using excess sulfur dioxide. A pressurized system is not essential to the reaction and passage of sulfur dioxide through a suspension of potassium cyanide in dry acetonitrile leads to the isolation of the same reaction products.

Preparation and Isolation of 3-Cyano-4-hydroxy-1,2,5-thiadiazole Salts.[25] **A. Open Vessel in Presence of Solvent.**—A suspension of vacuum-dried potassium cyanide (21.3 g.) in freshly distilled acetonitrile (200 ml.) was magnetically stirred in a dry flask fitted with condenser and calcium chloride guard tube. The suspension was treated with a slow stream of sulfur dioxide dried by passage through concentrated sulfuric acid and through a tower of anhydrous calcium sulfate. The reaction mixture gradually rose from room temperature to 73° and was accompanied by a change in color through bright yellow to sandy brown.

The suspended solid was collected and washed with acetonitrile and then ether. The pale yellow solid was identified by its infrared spectrum and by its X-ray powder pattern as predominantly potassium pyrosulfite. The colored filtrate slowly deposited a mass of pale yellow needles; these were collected and identified as the potassium salt of 3-cyano-4-hydroxy-1,2,5-thiadiazole (III).

Anal. Calcd. for C_3KN_3OS: C, 21.8; K, 23.7; N, 25.4; S, 19.41. Found: C, 22.2; K, 23.5; N, 26.1; S, 19.6.

On standing open to the atmosphere for 36 hr. the mother liquor deposited a further mass of crystals which were identified by infrared as the potassium acid salt.

B. Autogenous Pressure, in Presence of Solvent.—A 325-ml. Hastelloy B shaker tube, previously purged with nitrogen, was charged with potassium cyanide (21.5 g.), freshly distilled acetonitrile (200 ml.), and sulfur dioxide (24 g.). The tube was shaken and heated to 75° for 2 hr. The slight excess pressure was released from the cooled tube, and the finely divided suspension of inorganic material was removed from the product by filtration.

Concentration of the red acetonitrile solution gave a crystalline deposit. Recrystallization from ethanol furnished the pure potassium salt of 3-cyano-4-hyroxy-1,2,5-thiadiazole (4.85 g., 27% based on potassium cyanide).

Anal. Calcd. for C_3KN_3OS: C, 21.8; N, 25.4; S, 19.4. Found: C, 22.2; N, 25.3; S, 19.6.

C. Autogenous Pressure, in Absence of Solvent.—Powdered potassium cyanide (227 g.) was charged into a 1-l. stainless steel bomb previously purged with nitrogen; the bomb was cooled, evacuated, charged with sulfur dioxide (450 g., 100% theoretical excess), then heated with agitation at 60° for 4 hr. Excess sulfur dioxide was bled off from the cooled bomb and the tan-colored product (509 g.) removed and powdered through a 12-mesh sieve.

The product was transferred to a Soxhlet extraction apparatus and extracted with hot acetonitrile for 16 hr. The hot, colored extract was filtered to remove traces of insoluble inorganic material and concentrated to yield the crystalline thiadiazole, contaminated with a small amount of potassium thiocyanate. Recrystallization from ethanol (charcoal treatment) yielded the pure thiadiazole as the potassium acid salt (86.3 g., 51% based on potassium cyanide).

Anal. Calcd. for $C_3HN_3OS \cdot C_3KN_3OS$: C, 24.7; H, 0.35; K, 13.4; N, 28.8; S, 21.9; mol. wt., 292. Found: C, 24.8; H, 0.57; K, 13.5; N, 29.1; S, 22.0; mol. wt., 297 (titration).

The acid salt showed broad hydroxyl absorption in the infrared *ca.* 2.80 (Fig. 1), strong nitrile absorption at 4.45, and a wide plateau of high absorption from 8.0 to 11.0 μ. Characteristic absorption bands occurred at 11.05, 11.60, 11.75, 12.35, 12.55 13.15, and 13.25 μ. The ultraviolet absorption spectrum showed $\lambda_{max}^{H_2O}$ 213 mμ (ϵ 9330) and 335 (ϵ 8710).

Replacement of acetonitrile as the organic solvent by absolute ethanol yielded 3-cyano-4-hydroxy-1,2,5-thiadiazole in the form of its pure potassium salt, m.p. 305°.

Anal. Calcd. for C_3KN_3OS: C, 21.8; N, 25.4; S, 19.4. Found: C, 21.3; N, 25.1; S, 19.6.

Molecular weight determination in water showed dissociation into two fragments; mol. wt. actual 165; found 96.

The infrared spectrum (Fig. 1) showed major absorption bands at λ_{max}^{KBr} 4.48, 6.28, 6.35, 6.44, 7.09, 8.02, and doublets at 10.81, 10.87, 11.72, 11.82, 12.56, 12.64, and 13.09, 13.19 μ. The ultraviolet spectrum showed maxima at $\lambda_{max}^{H_2O}$ 212.5 mμ (ϵ 8510) and 334 (ϵ 8320).

(25) J. M. Ross and W. C. Smith, U. S. Patent 3,068,238 (1962).

Treatment of an aqueous solution of the potassium salt with salts of the following metals had no visible effect: Na, Ca, Ba, Cr^{III}, Mn^{II}, Co^{II}, Ni^{II}, Cu^{II}, Zn, Hg^{II}, and Pb^{II}.

The only water-insoluble metal salt isolated was the silver salt, which separated as a flocculent yellow-white precipitate on addition of silver nitrate.

Anal. Calcd. for C_3AgN_3OS: C, 15.4; N, 17.9; S, 13.7. Found: C, 15.7; N, 17.2; S, 13.6.

It showed an infrared spectrum indistinguishable from those of the alkali metal salts. Prolonged exposure to light led to gradual decomposition yielding a green-black residue.

3-Cyano-4-hydroxy-1,2,5-thiadiazole.—Suspension of the dry silver salt in ether and acidification with dry HCl gas caused precipitation of silver chloride. Removal of ether without heating gave almost quantitative yields of the cyanohydroxythiadiazole. Recrystallization from ether by slow evaporation *in vacuo* gave colorless chunky needles, m.p. 160–162°, resolidifying to the trimer which does not melt below 360°.

Anal. Calcd. for C_3HN_3OS: C, 28.4; H, 0.79; N, 33.1; S, 25.2; mol. wt., 127. Found: C, 28.5; H, 0.92; N, 33.4; S, 24.7; mol. wt. 127 (mass spec.); neut. equiv., 127; pK_a, 2.97.

A solution of the potassium acid salt (78.1 g.) in water (750 ml.) was treated with charcoal and the cold solution continuously extracted with ether for 16 hr. Evaporation of the dried ethereal extract gave the pure cyanohydroxythiadiazole (31.1 g., 92%), while evaporation of the aqueous solution yielded the potassium salt (43.5 g., 95%).

Acidification of aqueous solutions of the potassium salt or the potassium acid salt with concentrated hydrochloric acid, followed by continuous ether extraction, led to near quantitative isolation of the free cyanohydroxy compound.

Aqueous and ethanolic solutions of the cyanohydroxythiadiazole gave a red-brown color with ferric chloride. The infrared spectrum (Fig. 1) showed strong hydroxyl hydrogen-bonding in the 3.0–4.2 μ region, strong nitrile band at 4.45 μ, and occasional samples exhibited weak carbonyl absorption at 5.90 μ. The ultraviolet spectrum showed maxima at $\lambda_{max}^{H_2O}$ 213 mμ (ϵ 8710) and 334 (ϵ 8510) and λ_{max}^{EtOH} 297 (ϵ 7620) with a weak shoulder at 342 mμ which increased on dilution.

An O-methyl derivative was obtained by heating the silver salt suspended in acetone with excess methyl iodide for 12 hr.; the filtered solution gave a brownish, crystalline residue which separated from ethanol (charcoal) as colorless plates, m.p. 48.5–49.5°, $\lambda_{max}^{H_2O}$ 296 mμ (ϵ 11,480).

Anal. Calcd. for $C_4H_3N_3OS$: S, 22.7; OMe, 22.0. Found: S, 22.7; OMe, 21.5.

The same product was obtained on methylation with diazomethane.

Cyanohydroxythiadiazole metal salts were prepared by displacement reactions with a weak acid salt of the requisite metal. For example, an aqueous solution of cyanohydroxythiadiazole was treated with powdered lithium carbonate and warmed until all carbon dioxide was dispelled. Evaporation of the solution gave colorless needles of the thiadiazole lithium salt, m.p. >340°, which showed an infrared spectrum almost identical with that of the potassium salt. In a similar way evaporation of an aqueous mixture of equimolecular amounts of cyanohydroxythiadiazole and cupric acetate yielded an olive-green copper salt.

Tris(3-hydroxythiadiazolyl)-1,3,5-triazine.—The cyanohydroxy compound (5.0 g.) was heated for 15 min. at 180° in a slow stream of nitrogen; the solid completely melted, then recrystallized, forming a much brighter yellow mass. Traces of unchanged material sublimed onto cooler parts of the flask. The residual solid (5.0 g.) exhibited an infrared spectrum similar, but more complex, than that of the starting material, and exhibited no nitrile absorption at 4.5 μ. It did not melt below 360°.

The product was insoluble in ether, ethanol, and water, and remained unaffected on heating with 6 *N* hydrochloric acid for 2 hr. It was sparingly soluble (*ca.* 0.5%) in 1% aqueous alkali, forming a deep yellow solution which gelled on cooling. Acidification of the warm alkaline solution with dilute hydrochloric acid, or glacial acetic acid, regenerated the hydroxy compound. It dissolved in cold concentrated sulfuric acid, giving a golden yellow solution from which it was precipitated by dilution with water.

The triazine was slightly soluble in boiling nitrobenzene, from which it separated as a cream colored powder.

Anal. Calcd. for $(C_3HN_3OS)_3$: C, 28.4; H, 0.79; N, 33.1; S, 25.2. Found: C, 28.4; H, 1.05; N, 32.7; S, 25.1.

Attempted synthesis by condensation of 3-hydroxythiadiazole and cyanuric chloride in the presence of aluminum chloride in boiling tetrachloroethane gave no satisfactory product.

3-Hydroxy-1,2,5-thiadiazole-4-carboxamide.—A solution of potassium hydroxide (28 g.) in absolute ethanol (125 ml.) was added to a warm solution of the cyanohydroxythiadiazole potassium acid salt (29.2 g.) in absolute ethanol (600 ml.), and the clear solution was heated under gentle reflux for 3.5 hr. Ammonia was evolved and a pale yellow crystalline material separated out during the reaction. The mixture was cooled to 10° and the deposit collected, washed with ethanol and then ether, yielding the potassium salt of the amide (35.5 g., 96% yield).

Acidification of an aqueous solution of the potassium salt, followed by continuous extraction with ether and recrystallization of the extract from ethanol, gave the pure hydroxyamide as deep yellow needles, m.p. 175–177°. Strong primary amide absorption occurred in the infrared spectrum at 2.90, 3.07 (N—H), and 5.95 μ (C=O).

Anal. Calcd. for $C_3H_3N_3O_2S$: C, 25.8; H, 2.33; N, 29.0, S, 22.1. Found: C, 25.5; H, 2.23; N, 29.2; S, 22.4.

3-Hydroxy-1,2,5-thiadiazole-4-carboxylic Acid.—The cyanohydroxythiadiazole potassium acid salt (29.2 g.) in 200 ml. of water was treated with a solution of 28 g. of potassium hydroxide in 25 ml. of water and the clear solution heated under reflux for 2 hr. The cooled product was acidified with concentrated hydrochloric acid (60 ml.) and continuously extracted with ether for 16 hr. Ether was removed from the dried (Na_2SO_4) extract, yielding a colorless crystalline mass, m.p. 204–205° dec. (25.6 g., 88%). The purity of the product was not significantly improved by recrystallization from ethanol, or by vacuum sublimation.

Anal. Calcd. for $C_3H_2N_2O_3S$: C, 24.7; H, 1.38; N, 19.2; S, 21.9; neut. equiv., 146. Found: C, 24.8; H, 1.69; N, 18.9; S, 22.1; neut. equiv., 147; pK_{a_1} 2.57, pK_{a_2} 6.73.

Acidification of the saponification product with 45% sulfuric acid instead of concentrated hydrochloric acid usually caused the precipitation of a mass of pale yellow needles, which were recrystallized from water; m.p. 230° dec. The nature of this product was not proved, but ethereal extraction of its aqueous solution, acidified with hydrochloric acid, yielded the hydroxycarboxylic acid

Anal. Calcd. for $C_3HKN_2O_3S \cdot C_3H_2N_2O_3S$: C, 21.8; H, 0.91; K, 11.8; N, 16.9; S, 19.4. Found: C, 22.4; H, 1.35; K, 10.4; N, 16.8; S, 20.0.

3-Methoxy-1,2,5-thiadiazole-4-carboxylic Acid.—A sample of 3-cyano-4-methoxy-1,2,5-thiadiazole, m.p. 48.5–49.5°, was heated for 1 hr. with 10% aqueous KOH. The clear solution deposited colorless needles of the methoxycarboxylic acid on acidification, which recrystallized from ethanol; m.p. 165° dec., λ_{max}^{EtOH} 288 mμ (ϵ 8600).

Anal. Calcd. for $C_4H_4N_2O_3S$: OMe, 19.3. Found: OMe, 18.7.

Methyl 3-Methoxy-1,2,5-thiadiazole-4-carboxylate.—Methylation of the hydroxycarboxylic acid with diazomethane in ether solution gave the dimethyl derivative which crystallized from ethanol as cream needles, m.p. 76–77°, λ_{max}^{EtOH} 291 mμ (ϵ 9,300).

Anal. Calcd. for $C_5H_6N_2O_3S$: C, 34.5; H, 3.47; N, 16.1; OMe, 35.6. Found: C, 34.2; H, 3.66; N, 15.8; OMe, 35.1.

3-Hydroxy-1,2,5-thiadiazole-4-bromoimidate Hydrobromide.—A solution of cyanohydroxythiadiazole (2.54 g.) in 50 ml. of anhydrous ether containing 1.17 ml. of absolute ethanol was cooled to −20° and treated with a slow stream of anhydrous hydrogen bromide until there was no further increase in temperature (maximum +15°). The primrose-yellow precipitate (5.77 g.) was collected and air-dried. Solution in absolute ethanol followed by addition of excess ether gave no precipitate; concentration on a steam bath and dilution with ethyl acetate yielded a crystalline deposit, m.p. 161–167°, identified by infrared as the hydroxyamide. Treatment of the ether-insoluble salt with cold water regenerated the cyanohydroxy compound in 80% yield.

Methyl 3-Hydroxy-1,2,5-thiadiazole-4-carboxylate.—An ethereal solution of cyanohydroxythiadiazole (5.08 g.) and absolute methanol (5 ml.) was cooled to −20° and saturated with dry hydrogen chloride. After 24 hr. at room temperature the yellow crystalline deposit of the chloroimidate hydrochloride (7.4 g., 73%, m.p. 163–165°) was collected. A solution of 7.1 g. of chloroimidate in 30 ml. of methanol was treated with sodium methoxide (4.3 g.) in methanol. The solution was separated from precipitated sodium chloride after 0.5 hr., diluted with 200 ml. of water, and acidified with concentrated hydrochloric acid. The precipitated yellow solid (1.2 g., 21%) was recrystallized from methanol, m.p. 155–157° dec., and characterized as the hydroxythiadiazole methyl imidate ester.

Anal. Calcd. for $C_4H_5N_3O_2S$: C, 30.2; H, 3.17; N, 26.4; S, 20.2; OMe, 19.5. Found: C, 29.9; H, 3.16; N, 26.1; S, 19.9; OMe, 19.4.

The colored aqueous solution was extracted with ether, washed, and dried. The crystalline extract (2.7 g., 48%) of the hydroxythiadiazole methyl ester was recrystallized from a large volume of petroleum ether, giving colorless needles, m.p. 85.5–88°.

Anal. Calcd. for $C_4H_4N_2O_3S$: C, 30.0; H, 2.52; N, 17.5; S, 20.0. Found: C, 30.0; H, 2.49; N, 17.6; S, 20.5.

3-Hydroxy-1,2,5-thiadiazole. A.—Sublimed hydroxycarboxylic acid (22.5 g.) was suspended in 50 ml. of nitrobenzene, heated under gentle reflux in a stream of nitrogen for 2 hr., and allowed to cool. The dark brown product was filtered and the mass of brown crystals (12.5 g., 80%, m.p. 123–127°) collected and recrystallized from benzene and benzene–petroleum ether yielding cream needles, m.p. 128.5–130°. The infrared spectrum was reasonably similar to cyanohydroxythiadiazole but with no nitrile absorption. Strong hydroxyl hydrogen-bonding occurred at 2.8–4.2 μ and occasional samples exhibited weak carbonyl absorption at 5.82 μ. Major bands occurred at λ_{max}^{KBr} 6.50, 6.82, 7.20, 7.80, 8.30, 9.83, 11.50, 12.50, and 13.75 μ. The ultraviolet spectrum showed $\lambda_{max}^{H_2O}$ 276 mμ (ϵ 5300) with a shoulder at 300 mμ increasing on dilution.

Anal. Calcd. for $C_2H_2N_2OS$: C, 23.5; H, 1.97; N, 27.4; S, 31.4; neut. equiv., 102. Found: C, 23.7; H, 2.04; N, 27.4; S, 31.2; neut. equiv., 103; pK_a, 5.20.

B.—A suspension of 3-hydroxythiadiazole-4-carboxylic acid (5.0 g.) in 10 ml. of tetralin was heated at reflux for 1.5 hr.; the mixture became highly colored, and hydrogen sulfide was evolved. Half the filtrate was treated with 5 ml. of hot ethanolic picric acid (8%) from which needles of naphthalene picrate separated overnight, m.p. 150–151°. No naphthalene could be detected in the tetralin itself.

Diethylaminoacetamide. A. From 3-Hydroxy-1,2,5-thiadiazole.—A solution of the hydroxythiadiazole (4.07 g.) in 50% aqueous ethanol (50 ml.) was added to *ca.* 60 g. of freshly prepared Raney nickel in ethanol (250 ml.) and the mixture heated under gentle reflux for 1.5 hr. The cooled product was filtered and the ethanol solution evaporated under reduced pressure to yield a viscous yellow oil (1.20 g.). The residual pyrophoric nickel was extracted twice with boiling ethanol (200 ml.) which on evaporation gave a colorless, crystalline solid (0.5 g.), m.p. 49–50°. This product crystallized from ethanol–ether and finally *n*-hexane as long, colorless needles, m.p. 75.5–76.5°, undepressed on admixture with an authentic sample of diethylaminoacetamide and exhibiting an identical infrared spectrum.

Anal. Calcd. for $C_6H_{14}N_2O$: C, 55.4; H, 10.8; N, 21.5. Found: C, 55.3; H, 10.8; N, 21.4.

B. From Glycinamide.—A sample of glycinamide (0.37 g.), prepared by the method of Yang and Rising,[26] was heated under reflux with Raney nickel (*ca.* 8 g.) in 36 ml. of 90% aqueous ethanol for 1.5 hr. The colorless product was filtered hot and the pyrophoric nickel extracted once with boiling ethanol. Removal of solvent from the combined solutions gave a colorless oil (0.26 g.) having an infrared spectrum almost identical with that of the oil obtained by desulfurization of the thiadiazole. Extraction of the oil with boiling *n*-hexane (two 5-ml. portions) removed a quantity of crystalline material which recrystallized from *n*-hexane as colorless needles (30 mg.), m.p. 71.5–74°, and was identified by infrared comparison and mixture melting point as diethylaminoacetamide.

C. From Diethylaminoacetonitrile.—The corresponding nitrile (readily prepared from diethylamine and chloroacetonitrile[27]) was hydrolyzed by heating with concentrated sulfuric acid on a steam bath for 1 hr. The mixture was diluted with ethanol, neutralized by addition of potassium carbonate, and the free base obtained by addition of hot aqueous barium hydroxide. The filtrate was evaporated to dryness under reduced pressure and the residue extracted with boiling *n*-hexane which on cooling yielded colorless needles of diethylaminoacetamide, m.p. 75–76.5° (reported[28] m.p. 77°).

Pyrolysis of 3-Cyano-4-hydroxy-1,2,5-thiadiazole Potassium Salt.—Cyanohydroxythiadiazole potassium salt (1.65 g.) was

(26) P. S. Yang and M. M. Rising, *J. Am. Chem. Soc.*, **53**, 3183 (1931).
(27) L. Henry, *Rec. trav. chim.*, **24**, 173 (1905).
(28) A. Einhorn and A. Hamburger, *Ann.*, **361**, 122 (1908), footnote 10.

pyrolyzed by inserting the nitrogen-purged flask in a Woods metal bath at 345°. Evolved gases were led through solutions of (A) silver nitrate, (B) sodium sulfide, and (C) alkaline pyrogallol. The pale yellow crystalline solid gave a dark red-brown melt which slowly evolved gases, more rapidly as the temperature was increased during 20 min. to 395°, and maintained for a further 20 min. until no further gassing occurred.

No significant change occurred in silver nitrate solution (A); however, solution (B) gave positive tests for CN^- (Barnebey test[29]) and SCN^- (red with $FeCl_3$). Those gases which passed through (A) and (B) were totally absorbed by (C), giving a clear dark-brown solution indicative of oxygen absorption.

Traces of yellow sublimate above the solidified melt were shown to be sulfur by conversion to thiocyanate. The black residue (1.24 g.) was shown to include cyanide, cyanate, and thiocyanate and from the infrared spectrum probably para-cyanogen.

Hydrolysis of 3-Cyano-4-hydroxy-1,2,5-thiadiazole with 48% Hydrobromic Acid.—The cyanohydroxythiadiazole potassium acid salt (5 g.) was heated under gentle reflux with 48% hydrobromic acid (40 ml.) for 16.5 hr. A quantity of yellow crystalline sublimate in the condenser was identified as a mixture of ammonium bromide and sulfur. The clear dark brown reaction mixture deposited crystals of ammonium bromide and potassium bromide on cooling. The filtrate was extracted with ether, yielding a quantity of crude solid (300 mg.) which was characterized, *via* its calcium salt, as oxalic acid. Removal of HBr under reduced pressure gave a further yield of ammonium bromide, giving a total yield of 8.1 g. (82% theoretical amount for conversion of all three nitrogen atoms to ammonia).

Oxidative Degradation of the 1,2,5-Thiadiazole Nucleus. A. Oxidation with "Oxone" Monopersulfate Compound.[30]—A solution of cyanohydroxythiadiazole potassium acid salt (3.3 g.) in 25 ml. of water was added to a solution of "Oxone" monopersulfate compound (20 g., active oxygen 4.9%) in 75 ml. of water. The mixture was stirred at room temperature for 2 hr., then acidified with concentrated hydrochloric acid and continuously extracted with ether for 40 hr. The dried extract yielded 1.25 g. (44%) of oxalic acid monohydrate which was identified by infrared comparison of its calcium salt with an authentic sample. No other degradation product was detected.

B. Permanganate Oxidation of 3-Hydroxythiadiazole.—A stirred solution of 3-hydroxythiadiazole (2.55 g., 25 mmoles) in 100 ml. of water was treated during 0.5 hr. with a solution of potassium permanganate (8.0 g., 50 mmoles) in 125 ml. of water, such that the reaction temperature was 45 ± 3°. The final drops added required a finite time before decolorization was complete. The product was filtered and combined with two hot water (25 ml.) washings of the manganese dioxide residue. The pale yellow filtrate was concentrated to 50-ml. volume under reduced pressure and diluted with 500 ml. of ethanol. The precipitated white solid (3.45 g.) was contaminated with potassium sulfate and was purified by repeated recrystallization from water–ethanol. The pure product was obtained as colorless needles, identical, by comparative infrared analysis, with a sample of sulfamoyloxamic acid dipotassium salt kindly provided by Professor M. Carmack. The infrared spectrum was relatively simple, showing major absorption at λ_{max}^{KBr} 2.90, 6.05, 6.15, 7.40, 8.00, 8.13, 8.80, and 10.35 μ.

Anal. Calcd. for $C_2H_2K_2N_2O_5S$: C, 9.8; H, 0.82; K, 32.0; N, 11.5; S, 13.1. Found: C, 9.9; H, 1.08; K, 31.8; N, 11.4; S, 12.9.

In a similar experiment an intermediate oxidation product was isolated which was washed briefly with 6 *N* hydrochloric acid and recrystallized from water, giving colorless plates tentatively identified as the monopotassium salt of 3,4-dihydroxy-1,2,5-thiadiazole 1,1-dioxide. The infrared spectrum showed major absorption at λ_{max}^{KBr} 2.90, 5.65, 5.82, 5.98, 6.15, 7.40, 7.65, 8.65, 10.35, 11.78, and 13.25 μ.

Anal. Calcd. for $C_2HKN_2O_4S$: C, 12.8; H, 0.54; K, 20.8; N, 14.8; S, 17.1. Found: C, 12.5; H, 0.69; K, 20.4; N, 14.2; S, 17.0.

Reduction of 3-Cyano-4-hydroxy-1,2,5-thiadiazole. A. Sodium Borohydride Reduction.—Sodium borohydride (2.0 g., Metal Hydrides, Inc., 98+% pure) in 25 ml. of methanol was added dropwise to 2.0 g. of cyanohydroxy compound in 25 ml. of methanol, with the temperature maintained at <50°. The mixture was left at 25° for 1 hr. and evaporated to dryness under reduced pressure. Extraction of the residue with two 30-ml. portions of boiling ethanol gave 1.75 g. (73%) of unreacted thiadiazole as the sodium salt.

B. Sodium in Absolute Ethanol.—Cyanohydroxythiadiazole (2.54 g.) in 20 ml. of absolute ethanol was treated during 10 min. with a total of 1.8 g. of sodium metal. A vigorous reaction occurred with evolution of hydrogen sulfide. The mixture was heated under gentle reflux for 1 hr., cooled, and the sodium ethoxide decomposed by addition of 10 ml. of water. The solid, colored product (2.39 g.) was collected and identified by infrared spectrum as mainly the sodium salt of the hydroxyamide. Acidification of an aqueous solution of the product caused evolution of hydrogen sulfide and the amide, isolated as its silver salt, corresponded to a 57% yield as hydroxyamide.

Synthesis of 3-Cyano-4-hydroxy-1,2,5-thiadiazole. A. Isonitrosocyanoacetamide.—Using a modification of the procedure reported by Conrad and Schulze,[31] isonitrosocyanoacetamide was isolated as its potassium acid salt. A suspension of cyanoacetamide (16.8 g.) and potassium nitrite (20.4 g.) in 70 ml. of water was stirred, cooled to 4°, and treated all at one time with glacial acetic acid (24 ml.). After 0.5 hr. the yellow solution was removed from the ice bath and allowed to warm to room temperature. A mild exothermic reaction occurred, raising the reaction mixture to 42°, and shortly thereafter pale yellow needles of the potassium acid salt began to separate. After 1 hr. the product was cooled to 0° and the mass of needles (17.0 g., 68%) collected and washed well with chilled ethanol and ether. The product which gave a red color with alkaline ferrous sulfate was recrystallized once from hot water.

Anal. Calcd. for $C_6H_5KN_6O_4$: C, 27.3; H, 1.91; K, 14.8; N, 31.8. Found: C, 27.0; H, 1.89; K, 14.8; N, 31.5.

The potassium salt of isonitrosocyanoacetamide was obtained by treating a hot aqueous solution of the potassium acid salt with the calculated amount of potassium hydroxide. The pure product was extremely soluble in water and required recrystallization from 1:4 water–ethanol. It separated as deep golden yellow needles, m.p. 269° dec.

Anal. Calcd. for $C_3H_2KN_3O_2$: K, 25.9. Found: K, 25.7.

Acidification of aqueous solutions of either of the above salts followed by extraction with ether yielded, upon evaporation, the free isonitroso compound which separated from ethyl acetate as colorless, irregular plates, m.p. 181–182° dec. (reported[31] m.p. 184°).

Anal. Calcd. for $C_3H_3N_3O_2$: C, 31.9; H, 2.67. Found: C, 31.7; H, 2.55.

B. 3-Cyano-4-hydroxy-1,2,5-thiadiazole.—A solution of isonitrosocyanoacetamide (6.18 g.) in 30 ml. of acetonitrile at 50° was treated dropwise during 5 min. with a solution of sulfur dichloride (17 ml.) in 25 ml. of acetonitrile. Considerable evolution of hydrogen chloride occurred, with a gradual rise in temperature, and the deep red sulfur dichloride color was dispelled to pale yellow. The mixture was heated under reflux for 1 hr. and the clear solution then evaporated to dryness under reduced pressure. The yellow crystalline residue was dissolved in ether (200 ml.), washed with water (five 25-ml. portions), and dried. The ethereal solution was concentrated to 10-ml. volume, whence large orange needles (3.9 g.) separated. The crude cyanohydroxythiadiazole was purified *via* its silver salt and crystallized from ether as pale yellow microcrystals, m.p. 157–160°, followed by resolidification. Its infrared spectrum was identical with that of samples of the cyanohydroxythiadiazole derived from the KCN–SO_2 product.

Anal. Calcd. for C_3HN_3OS: C, 28.3; H, 0.79; N, 33.1. Found: C, 27.8; H, 0.78; N, 32.4.

The product was further purified by conversion to the potassium salt which crystallized from ethanol as yellow needles.

Anal. Calcd. for C_3KN_3OS: C, 21.8; N, 25.4. Found: C, 21.7; N, 25.8.

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