708. *Antituberculosis Agents. Part III.* Pyridine-4-sulphonamides and -sulphonhydrazides.*

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Pyridine-4-sulphonamide and -sulphonhydrazide, and numerous derivatives of these, have been prepared. Pyridine-4-sulphonamide has little antibacterial activity, and none of the derivatives of pyridine-4-sulphonhydrazide has significant activity against *Myco. tuberculosis*.

Pyridine-4-sulphonhydrazide, the analogue of *iso*nicotinic acid hydrazide (isoniazid), and pyridine-4-sulphonamide were required for examination of their antituberculosis activity. King and Ware [1] failed to obtain the latter, being unable to prepare the sulphonyl chloride. They reported that sodium pyridine-4-sulphonate with phosphorus pentachloride gave 1 : 4-dihydro-4-imino-1-4'-pyridylpyridine or 1-4'-pyridyl-4-pyridone, together with phosphorus oxychloride and thionyl chloride. 4-Pyridthione with bromine in acetic acid [2] gave di-4-pyridyl disulphide, and with chlorine gave 4-chloropyridine and di-4-pyridyl sulphide. Intermediate formation of unstable pyridine-4-sulphonyl halide would account for all these products. We therefore tried, by modified procedures, to isolate the sulphonyl chloride. Since the end of our work, we found that Talik and Plazek [2] had prepared pyridine-4-sulphonamide, the related dimethylamide and 1-*iso*propylidene-2-pyridine-4'-sulphonylhydrazine by methods essentially similar to ours.

Chlorination of 4-pyridthione in glacial acetic acid (cf. Lee and Dougherty [3]) and treatment of the solution with ammonia gave di-4-pyridyl sulphide as described by King and Ware.[1] Attempts to precipitate the acid chloride hydrochloride were unsuccessful. The relatively high freezing point of glacial acetic acid would not permit reaction below 15°, but limited chlorination (10 min.) at 0° in concentrated hydrochloric acid [4] and treatment with ammonia gave di-4-pyridyl disulphide. More prolonged chlorination (2 hr.) under the same conditions, and evaporation at room temperature *in vacuo*, however, gave pyridine-4-sulphonic acid,[5] confirming the intermediate formation of the sulphonyl chloride. Pyridine-4-sulphonamide was however obtained by prolonged chlorination of 4-thiopyridone in concentrated hydrochloric acid at 0° and pouring of the product solution into aqueous ammonia. The identity of the product was confirmed by preparaton of a picrate and *N*-oxide (Naito *et al.*[4]). Contrary to the observations of Talik and Plazek [2] we find that the chlorination of 4-pyridthione to pyridine-4-sulphonyl chloride does not require the presence of 30% hydrogen peroxide.

An attempt to extend the above method to pyridine-4-sulphonhydrazide gave 4-pyridylhydrazine hydrochloride, probably arising from the sulphonhydrazide (unstable—see below), under the alkaline reaction conditions which obtain in the presence of excess of hydrazine. Nitrobenzene-*o*- and -*p*-sulphonamide and pyridine-2- and -4-sulphonamide 1-oxide [4] undergo comparable rearrangements with loss of sulphur dioxide in alkaline solution.

To avoid separation of a water-soluble and labile product from large amounts of hydrazine hydrochloride, we attempted isolation of the intermediate pyridine-4-sulphonyl chloride. Freeze-drying the chlorinated solution at −30° proved difficult owing to the high concentration of hydrochloric acid present. Reaction of the concentrate with hydrazine hydrate gave 4-pyridylhydrazine hydrochloride, 4-pyridylhydrazinium pyridine-4-sulphonate, and small quantities of two other products, which were not identified. More

* Part II, *J.*, 1956, 3892.

[1] King and Ware, *J.*, 1939, 873.
[2] Talik and Plazek, *Acta Polon. Pharm.*, 1955, **12**, 5, 179; *Chem. Abs.*, 1957, **51**, 17,911.
[3] Lee and Dougherty, *J. Org. Chem.*, 1940, **5**, 81.
[4] Caldwell and Kornfeld, *J. Amer. Chem. Soc.*, 1942, **64**, 1695; Naito and Dohmori, *Pharm. Bull.* (*Japan*), 1955, **3**, 38.
[5] Comrie and Stenlake, *J.*, 1958, 1853.

rapid concentration of the chlorinated solution at 0°, and treatment with hydrazine hydrate, yielded hydrazine sulphate as the only identifiable product. Pyridine-4-sulphonyl chloride was finally isolated as an oil from the chlorination of 4-thiopyridone in concentrated hydrochloric acid at 0° by neutralisation with calcium carbonate and rapid extraction into chloroform. Reaction of this solution with anhydrous hydrazine gave pyridine-4-sulphonhydrazide, whose identity was confirmed by its ability to reduce cold ammoniacal silver nitrate solution, and by the preparation of a picrate and other derivatives. Pyridine-4-sulphonhydrazide slowly decomposes in the solid state at room temperature, and more rapidly in solution in water, methanol, or ethanol even at 0°.

Alkyl,[7] alkylidene,[8] and aralkylidene [9] derivatives of *iso*nicotinoylhydrazine, not only retain the same level of antituberculosis activity, but also are less toxic than the parent compound. The 1-alkylidene- and 1-aralkylidene-2-pyridine-4′-sulphonylhydrazines listed in Table 1 have been prepared and, except for the ethylidene derivative, are stable in

TABLE 1. 1-*Alkylidene and* 1-*aralkylidene-2-pyridine-4′-sulphonylhydrazines.*

1-Substituent	M. p. (decomp.)	Yield (%)	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
Ethylidene	120°	42	$C_7H_9O_2N_3S$	42·5	4·1	42·2	4·55
*iso*Propylidene	147	59	$C_8H_{11}O_2N_3S$	45·5	5·2	45·1	5·2
1-Phenylethylidene	148—149	76	$C_{13}H_{13}O_2N_3S$	57·0	4·7	56·7	4·8
2-Phenylethylidene	118	80	$C_{13}H_{13}O_2N_3S$	56·9	4·5	56·7	4·8
*cyclo*Hexylidene	142	75	$C_{11}H_{15}O_2N_3S$	52·4	5·7	52·2	6·0
*cyclo*Heptylidene	166	86	$C_{12}H_{17}O_2N_3S$	54·0	6·2	53·9	6·4
Benzylidene	141—142	88	$C_{12}H_{11}O_2N_3S$	55·3	4·2	55·2	4·3
p-Hydroxybenzylidene	168—169	71	$C_{12}H_{11}O_3N_3S$	51·9	4·0	52·0	4·0
p-Methoxybenzylidene	155—156	86	$C_{13}H_{13}O_3N_3S$	54·0	4·2	53·6	4·5
Salicylidene	166	89	$C_{12}H_{11}O_3N_3S$	52·1	4·3	52·0	4·0
Vanillylidene	120—121	65	$C_{13}H_{13}O_4N_3S$	51·3	4·7	50·8	4·3
Piperonylidene	163—164	83	$C_{13}H_{11}O_4N_3S$	51·5	3·8	51·2	3·6
p-Dimethylaminobenzylidene	180	76	$C_{14}H_{16}O_2N_4S$	55·4	5·4	55·3	5·3
m-Methylbenzylidene	136—137	77	$C_{13}H_{13}O_2N_3S$	56·9	4·8	56·7	4·8
Cinnamylidene	148	89	$C_{14}H_{13}O_2N_3S$	58·8	4·5	58·5	4·6
Veratrylidene	164—165	65	$C_{14}H_{15}O_4N_3S$	52·1	4·2	52·3	4·7
Hexahydro-2 : 4 : 6-trioxo-5-pyrimidylidene	>360	99	$C_9H_7O_5N_5S,H_2O$	34·5	3·2	34·3	2·9
D-Glucosyl *	156	50	$C_{11}H_{17}O_7N_3S$	39·4	5·0	39·4	5·1
$CH_2(CMe{:}N{\cdot}NHX)_2$ †	162—163	92	$C_{15}H_{18}O_4N_6S_2$	N = 20·5		N = 20·5	

* Structure of sugar residue uncertain, but probably cyclic. † Product from acetylacetone.

TABLE 2. 1-*Acyl-2-pyridine-4′-sulphonylhydrazines.*

Acyl	M. p. (decomp.)	Yield (%)	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
Acetyl	181—182°	65	$C_7H_9O_3N_3S$	39·2	3·7	39·1	4·2
Benzoyl	164 *	40	$C_{12}H_{11}O_3N_3S$	51·9	4·0	52·0	4·0
β-Hydroxycarbonylpropionyl	179—180	73	$C_9H_{11}O_5N_3S$	39·4	4·3	39·6	4·1
o-Hydroxycarbonylbenzoyl	158	60	$C_{13}H_{11}O_5N_3S$	49·0	3·3	48·6	3·45
β-Hydroxycarbonylacryloyl	166—167	86	$C_9H_9O_5N_3S$	40·1	3·3	39·9	3·35
*iso*Nicotinoyl	120—121	20	$C_{12}H_{14}O_4N_4S$ †	46·3	4·5	46·45	4·55
Benzenesulphonyl	142—143	40	$C_{11}H_{11}O_4N_3S_2$	42·3	3·7	42·2	3·5
p-Toluenesulphonyl	153—154	40	$C_{12}H_{13}O_4N_3S_2$	44·0	4·0	44·0	4·0
Pyridine-4′-sulphonyl	173—174	60	$C_{10}H_{10}O_4N_4S_2$	38·5	3·6	38·2	3·2

* After drying *in vacuo*. The hemihydrate (from water) has m. p. 128—129°. † Found: N, 17·7. Reqd.: N, 18·1%.

the solid state and in solution. Contrary to Talik and Plazek,[2] we find that the 2-*iso*propylidene compound readily forms a picrate. Attempts to prepare the 4-pyridylmethylene and the furfurylidene derivative were unsuccessful, but the latter was obtained as its picrate.

[6] Naito, Dohmori, and Shimoda, *Pharm. Bull.* (*Japan*), 1955, **3**, 34.
[7] Fox and Gibas, *J. Org. Chem.*, 1953, **18**, 994; Fox, *ibid.*, p. 990.
[8] Fox and Gibas, *ibid.*, p. 983.
[9] Bavin, Drain, Seiler, and Seymour, *J. Pharm. Pharmacol.*, 1952, **4**, 844.

The 1-acyl-2-pyridine-4'-sulphonylhydrazines listed in Table 2 have also been prepared (cf. Fox and Gibas [10]) from the sulphonhydrazide and acid anhydride. 1-Phenylcarbamoyl- and 1-allylthiocarbamoyl-2-pyridine-4'-sulphonylhydrazine were obtained by condensation with phenyl *iso*cyanate and allyl *iso*thiocyanate respectively. The sulphonhydrazide with ethyl acetoacetate gave 3-methyl-1-pyridine-4'-sulphonyl-5-pyrazolone, and with acetylacetone gave 2 : 4-di(pyridine-4'-sulphonamidoimino)pentane rather than the expected pyrazole.

Condensation of pyridine-4-sulphonhydrazide with benzene-, toluene-*p*-, and pyridine-4-sulphonyl chloride yielded 1 : 2-disulphonylhydrazines. 1 : 2-Di(pyridine-4'-sulphonyl)-hydrazine could not, however, be obtained directly from hydrazine and excess of pyridine-4-sulphonyl chloride (see Dann and Davies [11]).

Attempts to reduce the *iso*propylidene and benzylidene derivative to the *iso*propyl and benzyl derivative catalytically and with sodium borohydride were unsuccessful. Condensation of the sodio-derivative of pyridine-4-sulphonhydrazide with benzyl chloride also failed to yield the required compound, giving instead benzyl 4-pyridyl sulphone.[12]

Although possibly an alternative route to pyridine-4-sulphonhydrazide, reaction of the sulphonamide with an excess of hydrazine for a limited time gave a crystalline product, tentatively identified as ammonium 4-pyridylhydrazinium thiosulphate, and equimolar proportions in dry methanol gave after 6½ hr. also 4-pyridylhydrazinium pyridine-4-sulphonate.

We thank Dr. E. O. Morris of this College for the bacteriological examination of pyridine-4-sulphonamide which was bacteriostatic against a wide range of Gram-positive and Gram-negative organisms only at concentrations greater than 1 in 1000; also Dr. S. R. M. Bushby of the Wellcome Research Laboratories for the preliminary bacteriological examination of the derivatives of pyridine-4-sulphonhydrazide listed in Tables 1 and 2: against *Myco. tuberculosis* var. hominis (CN3679) both in Dubos and Davies's medium [13] and in the egg-agar solid medium of Peizer and Schecter,[14] none showed significant activity.

Experimental

We thank Mr. W. McCorkindale and Dr. A. C. Syme for the microanalyses.

Pyridine-4-sulphonamide.—(*a*) 4-Pyridthione (1·11 g.) in concentrated hydrochloric acid (7·5 ml.) and water (2 ml.), cooled to −10°, was chlorinated at such a rate as to keep the temperature at about −5°. After the end of chlorination, the mixture was poured on ice (15 g.), and the slurry transferred to ice-cold ammonia (40 ml.; *d* 0·88). The mixture was kept at room temperature for 3 hr., then concentrated in a vacuum until solid began to separate, and next cooled at 0° overnight; it yielded *pyridine-4-sulphonamide* as rhombic prisms (0·91 g., 58%), m. p. 172—173° (from ethanol or water) (Found: C, 38·3; H, 3·5; N, 17·5. $C_5H_6O_2N_2S$ requires C, 38·0; H, 3·8; N, 17·7%).

(*b*) 4-Pyridthione (1·11 g.) was chlorinated as in (*a*), and the solution was treated with calcium carbonate (*ca.* 1 g. to part-neutralise acid and displace dissolved chlorine) and poured into ice-cold chloroform (20 ml.). Calcium carbonate (*ca.* 7 g.) was carefully added, with shaking, at −5°, to complete the neutralisation. After being shaken vigorously the clear chloroform solution was decanted from the almost solid white sludge, which was then washed further with cold chloroform (2 × 20 ml.). The combined chloroform solutions were dried (Na_2SO_4) at 0—5° and filtered, and dry ammonia gas passed into the filtrate for 10 min. After cooling, the precipitated product (0·93 g., 60%) was filtered off and recrystallised, to yield pyridine-4-sulphonamide, m. p. 172—173° (from water). Its *picrate* (plates) had m. p. 186—187° (decomp.) (from ethanol) (Found: C, 34·3; H, 1·9; N, 17·9. $C_{11}H_9O_9N_5S$ requires C, 34·1; H, 2·3; N, 18·0%).

Pyridine-4-sulphonamide 1-*Oxide.*—Pyridine-4-sulphonamide (0·158 g.) was heated with 30%

[10] Fox and Gibas, *J. Org. Chem.*, 1953, **18**, 1375.
[11] Dann and Davies, *J.*, 1929, 1050.
[12] Carpino, *J. Amer. Chem. Soc.*, 1957, **79**, 4427.
[13] Dubos and Davies, *J. Exp. Med.*, 1946, **83**, 409.
[14] Peizer and Schecter, *Amer. J. Clin. Path.*, 1950, **20**, 682.

hydrogen peroxide (0·3 ml.) and glacial acetic acid (0·4 ml.) at 70—80° for 5 hr. Concentration in a vacuum gave a brown solid (0·085 g., 49%) which recrystallised from ethanol (5 ml.; charcoal) to yield pyridine-4-sulphonamide 1-oxide, m. p. 230° (decomp.). Naito and Dohmori [4] give m. p. 228°.

Pyridine-4-sulphonanilide.—4-Pyridthione (1·11 g., 0·01 mole) was converted into pyridine-4-sulphonyl chloride as in (*b*), and the cold, dry chloroform solution of the latter shaken with aniline (1·86 g., 0·02 mole), left overnight at 0°, filtered, and evaporated under reduced pressure. The residual oil recrystallised from methanol (60%) as needles (1·48 g., 65%) of *pyridine-4-sulphonanilide*, m. p. 135—136° (Found: N, 12·1. $C_{11}H_{10}O_2N_2S$ requires N, 12·0%).

Pyridine-4-sulphonhydrazide.—Batches of 4-pyridthione (5·55 g., 0·05 mole) were chlorinated as in (*b*) above. Addition of the cold, dry chloroform solution of pyridine-4-sulphonyl chloride in 10—20 ml. portions to anhydrous hydrazine (3·2 g., 0·1 mole) with shaking caused deposition of colourless crystals. The mixture was left overnight at 0°, then filtered, and the residue was washed with ether and dried *in vacuo*. The crude product was suspended in ice-cold water (15 ml.), quickly filtered, washed with ice-cold water (5 × 1 ml.), and dried *in vacuo* (sulphuric acid), yielding *pyridine-4-sulphonhydrazide* (6·3 g., 73%) as needles, m. p. 95—96° (from ice-cold water or methanol) (Found: C, 35·0; H, 3·7; N, 24·5; S, 18·2. $C_5H_7O_2N_3S$ requires C, 34·7; H, 4·1; N, 24·3; S, 18·5%). It gave a *picrate* (from ethanol), m. p. 117—118° (Found: C, 32·9; H, 2·31; N, 20·7. $C_{11}H_{10}O_9N_6S$ requires C, 32·8; H, 2·5; N, 20·9%), *dihydrochloride* (from methanol), m. p. 122—123° (Found: C, 25·7; H, 4·8; S, 11·7. $C_5H_9O_2N_3Cl_2S,CH_3{\cdot}OH$ requires C, 25·9; H, 4·7; S, 11·5%), and *sodio-derivative* (by treatment with sodium ethoxide), m. p. *ca.* 285° (Found: C, 30·3; H, 3·8; Na, 11·8. $C_5H_6O_2N_2SNa$ requires C, 30·8; H, 3·1; Na, 11·8%). Pyridine-4-sulphonhydrazide is insoluble in benzene, ether, and chloroform, sparingly soluble in alcohol, and soluble in methanol and water. Aqueous solutions slowly become yellow with evolution of nitrogen, even at 0°; similar decomposition occurs in hot methanol. The solid slowly becomes yellow and a pyridine-like odour develops.

1-*Alkylidene- and* 1-*Aralkylidene-2-pyridine-4'-sulphonylhydrazines.*—Pyridine-4-sulphonhydrazide (0·865 g., 0·005 mole), suspended in methanol (5 ml.), was shaken with aldehyde or ketone (0·005 mole) and sufficient methanol to give a homogeneous solution. The crystalline *products* which separated (if necessary after concentration of the solution) recrystallised from ethanol, methanol, or mixtures of these with water. Constants and analyses are recorded in Table 1.

1-*Ethylidene-2-pyridine-4'-sulphonylhydrazine picrate* was obtained as needles (from ethanol), m. p. 113° (Found: C, 36·6; H, 2·4. $C_{13}H_{12}O_9N_6S$ requires C, 36·5; H, 2·8%). The *picrate* of the *iso*propylidene analogue formed prisms (from methanol), m. p. 135—136° (decomp.) (Found: C, 38·2; H, 3·1; N, 19·2. $C_{14}H_{14}O_9N_6S$ requires C, 38·0; H, 3·2; N, 19·0%), and that of the furfurylidene compound prisms (from ethanol), m. p. 161° (decomp.) (Found: C, 40·5; H, 2·2; N, 17·4. $C_{16}H_{12}O_{10}N_6S$ requires C, 40·0; H, 2·5; N, 17·5%).

1-*Phenyl-2-pyridine-4'-sulphonylhydrazine.*—4-Pyridthione (1·11 g., 0·01 mole) was converted into pyridine-4-sulphonyl chloride as before, and the cold dry chloroform solution of the latter shaken with phenylhydrazine (2·16 g., 0·02 mole) in chloroform (10 ml.), then left overnight at 0°; the product was separated, washed with chloroform, dried *in vacuo*, then washed free from chloride with ice-cold water, and recrystallised from ethanol to yield 1-*phenyl-2-pyridine-4'-sulphonylhydrazine* (0·3 g., 12%), m. p. 145° (decomp.) (Found: N, 16·7. $C_{11}H_{11}O_2N_3S$ requires N, 16·9%).

1 : 1-*Diacetyl-2-pyridine-4'-sulphonylhydrazine.*—Pyridine-4-sulphonhydrazide (0·865 g.) was added in small portions to acetic anhydride (5 ml.), with shaking and gentle warming until complete solution was effected. On cooling, the *diacetyl compound* (0·96 g., 69%) separated as colourless prisms, m. p. 161° (decomp.) (Found: C, 42·1; H, 3·7; S, 12·4. $C_9H_{11}O_4N_3S$ requires C, 42·0; H, 4·3; S, 12·45%).

1-*Acyl-2-pyridine-4'-sulphonylhydrazines.*—Pyridine-4-sulphonhydrazide (0·865 g., 0·005 mole), suspended in methanol (5 ml.) or dry dioxan, was shaken with the acid anhydride (0·005 mole) and sufficient solvent to give a homogeneous solution. The crystalline products which separated were recrystallised from ethanol or methanol. Constants and analyses are in Table 2.

1-*Benzoyl-2-pyridine-4'-sulphonylhydrazine hydrochloride* had m. p. 194° (decomp.) (Found: C, 45·9; H, 3·7. $C_{12}H_{12}O_3N_3ClS$ requires C, 45·8; H, 3·9%).

1-*Phenylcarbamoyl-2-pyridine-4'-sulphonylhydrazine.*—Pyridine-4-sulphonhydrazide (0·865

g., 0·005 mole), suspended in methanol (5 ml.), was treated with phenyl *iso*cyanate (0·6 g.) in methanol (5 ml.). When shaken, the mixture became homogeneous and almost immediately deposited the *phenylcarbamoyl derivative* (1·2 g., 80%) as prisms, m. p. 200° (decomp.) (Found: N, 19·1. $C_{12}H_{12}O_3N_4S$ requires N, 19·2%).

1-*Allylthiocarbamoyl*-2-*pyridine*-4′-*sulphonylhydrazine*.—Pyridine-4-sulphonhydrazide (0·865 g., 0·005 mole), suspended in methanol (5 ml.), was treated with allyl *iso*thiocyanate (0·49 g.) in methanol (2 ml.). The *product* (0·35 g., 25%), which separated overnight at 0° and on subsequent concentration, was obtained as prisms, m. p. 149° (decomp.), from methanol (Found: N, 20·6. $C_9H_{12}O_2N_4S_2$ requires N, 20·6%).

1-*Benzenesulphonyl*-2-*pyridine*-4′-*sulphonylhydrazine*.—Pyridine-4-sulphonhydrazide (0·432 g., 0·0025 mole) was treated dropwise with benzenesulphonyl chloride (0·44 g., 0·0025 mole) in dry pyridine (5 ml.), with cooling, and stirred until solution was complete. Ice-cold water (15 ml.) was then slowly added, and the *product* collected and recrystallised as needles (0·31 g.) (from ethanol), m. p. 142—143° (decomp.) (see Table 2 for analytical data).

1-Pyridine-4′-sulphonyl-2-toluene-*p*-sulphonylhydrazine was prepared similarly.

1 : 2-*Di*(*pyridine*-4′-*sulphonyl*)*hydrazine*.—Pyridine-4-sulphonhydrazide (0·865 g.) in dry pyridine (10 ml.) was treated with pyridine-4-sulphonyl chloride [from 4-pyridthione (1 g.)] in chloroform, with cooling. The product which separated overnight at 5° was filtered off, washed with ether, suspended in water (10 ml.), filtered off, and dried *in vacuo*, to yield 1 : 2-*di*(*pyridine*-4′-*sulphonyl*)*hydrazine* (0·95 g.), m. p. 173—174° (decomp.) (from dimethylformamide–ethanol) (see Table 2).

3-*Methyl*-1-(*pyridine*-4′-*sulphonyl*)-5-*pyrazolone*.—Pyridine-4-sulphonhydrazide (0·173 g., 0·001 mole) in methanol (1 ml.) was shaken with ethyl acetoacetate (0·13 g., 0·001 mole) in methanol (1 ml.) and left overnight at 0°. The *pyrazolone* (0·18 g., 75%) was deposited as needles, m. p. 124—125° (from methanol) (Found: N, 17·7. $C_9H_9O_3N_3S$ requires N, 17·6%).

Benzyl 4-Pyridyl Sulphone.—Pyridine-4-sulphonhydrazide (0·865 g., 0·005 mole) was added in small amounts to sodium (0·23 g., 0·01 g.-atom) in ethanol (10 ml.), and benzyl chloride (1·28 g., 0·01 mole) was added rapidly before the monosodio-derivative separated. The solution was refluxed for 4 hr. on a water-bath, cooled, filtered to remove sodium chloride, and concentrated, to yield the *sulphone* (0·25 g.) in plates, m. p. 169—170° (decomp.) (from aqueous methanol) (Found: C, 61·2; H, 4·6; N, 6·1. $C_{12}H_{11}O_2NS$ requires C, 61·8; H, 4·7; N, 6·0%).

Reaction of Pyridine-4-Sulphonamide with Hydrazine.—(*a*) Pyridine-4-sulphonamide (0·79 g.) was heated with anhydrous hydrazine (0·9 g.) on a boiling-water bath for 30 min. After a few minutes the mixture separated into two layers, but it became homogeneous on further heating, with evolution of ammonia and gentle intermittent bubbling. Evaporation under reduced pressure gave colourless needles (0·7 g.), m. p. 161° (decomp.) (from methanol) (Found: C, 24·8; H, 5·4; N, 24·0. $C_5H_{12}O_3N_4S_2$ requires C, 25·0; H, 5·0; N, 23·3%). The product, probably *ammonium 4-pyridylhydrazinium thiosulphate*, when treated with dilute hydrochloric acid, liberated sulphur dioxide and colloidal sulphur; extraction of the latter with carbon disulphide and evaporation of the aqueous solution gave 4-pyridylhydrazine hydrochloride, m. p. 241° (decomp.) (from ethanol). Koenigs, Weiss, and Zscharn [15] give m. p. 238°. An aqueous solution of the product gave a white precipitate with lead acetate (Found: Pb, 65·9. PbS_2O_3 requires Pb, 64·9%). With sodium hydroxide no ammonia could be detected, but an oil insoluble in the common organic solvents was produced, and on exposure to air a deep pink colour developed. 4-Pyridylhydrazine beomes pink in air.

(*b*) Pyridine-4-sulphonamide (0·79 g.) and anhydrous hydrazine (0·16 g.) in methanol (10 ml.) were refluxed until no more ammonia was evolved (*ca.* 7 hr.). Cooling and storage for 3 days gave a product (0·62 g.), identical with that obtained in (*a*). Concentration of the mother-liquors gave a yellow substance (0·2 g.), m. p. 130—170° which on repeated crystallisation from methanol yielded *4-pyridylhydrazinium pyridine*-4′-*sulphonate*, m. p. 226—227° (decomp.) (Found: C, 44·3; H, 4·2; N, 20·7. $C_{10}H_{12}O_3N_4S$ requires C, 44·8; H, 4·5; N, 20·9%). An aqueous solution passed through a column of Deacidite FF gave an eluate, which, on acidification with dilute hydrochloric acid and evaporation, yielded 4-pyridylhydrazine hydrochloride, m. p. 241° (decomp.) (from aqueous ethanol).

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[15] Koenigs, Weiss, and Zscharn, *Ber.*, 1926, **59**, 316.