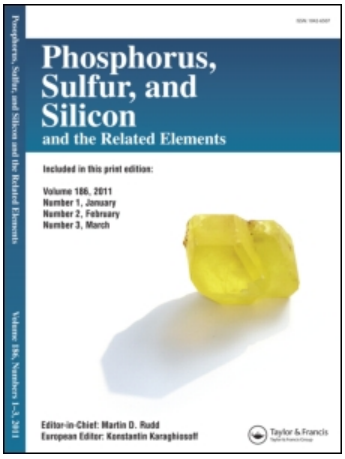

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SOME REACTIONS OF PYRIDINE-3-SULFONYL CHLORIDE

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The hydrochloride of pyridine-3-sulfonyl chloride (**1**) with hydrazine gave the hydrazide (**2**), from which a semicarbazide (**15**) and a series of hydrazones (**4–14**) were obtained. The chemical shifts of the NH protons of the hydrazones were correlated with the Hammett σ-constants of the substituents. With sodium azide, the sulfonyl chloride (**1**) gave the azide (**16**) which reacted with both norbornene and triphenylphosphine. The sulfonyl chloride (**1**) was hydrolysed to the sulfonic acid (3) by boiling with ethanol. Reaction of the hydrazide (**2**) with β-diketones afforded the pyrazoles (**19a–22a**). The intermediate sulfonohydrazones (**19–22**) were isolated in each case; however the product with ethyl acetoacetate (**26**) could not be cyclised to the pyrazole. The mass spectra of the pyrazoles are briefly discussed.

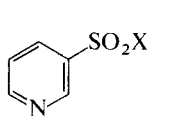
INTRODUCTION

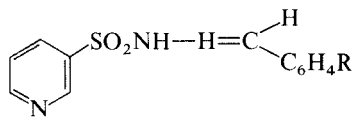
We previously reported[1] the reactions of quinoline-8-sulfonyl chloride with hydrazine, phenylhydrazine and sodium azide, and have continued the investigation of the reactions of N-heteroaromatic sulfonyl chlorides in our search for potential biocides. Pyridine-3-sulfonyl derivatives may react with diphosphopyridine nucleotide (DPN) to form the pyridine sulfonyl analogues which could function as cell inhibitors of DPN (cf. Ref. 2). Pyridine-2- and 4-sulfonyl chlorides are unstable,[3] but the 3-sulfonyl chloride (**1**) can be isolated as a stable hydrochloride.[4,5] As sulfonohydrazides and hydrazones have been shown[6,7] to possess fungicidal activity, several derivatives of pyridine-3-sulfonohydrazide (**2**) have been prepared for biological evaluation.

Derivatives of Pyridine-3-Sulfonyl Chloride

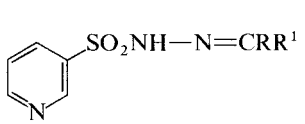
Reaction of pyridine-3-sulfonic acid (**3**) with phosphorus pentachloride gave the sulfonyl chloride (**1**), which was isolated in good yield as the hydrochloride,[4] and was converted to the sulfonohydrazide (**2**) with an excess of hydrazine hydrate.[5]

The pyridine-3-sulfonohydrazones (**4–14**) were readily prepared by condensation with the appropriate carbonyl compounds and were characterized by m.p., microanalysis, and i.r. and n.m.r.

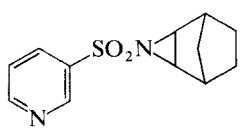




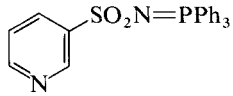
X		*R*		*R*	
(**1**)	Cl	(**4**)	H	(**9**)	*p*-OH
(**2**)	$NHNH_2$	(**5**)	*p*-NO_2	(**10**)	*p*-NMe_2
(**3**)	OH	(**6**)	*m*-Cl	(**11**)	*p*-Cl
(**15**)	$NHNHCONHCH_3$	(**7**)	*p*-Me	(**12**)	*p*-Ph
(**16**)	N_3	(**8**)	*p*-OMe	(**13**)	*o*-NO_2



(**14**)



(**17**)



(**18**)

spectra. The n.m.r. spectra showed a broad high-frequency signal between δ10.1 and δ12.3, which disappeared on treatment with D_2O and could therefore be unambiguously assigned to the NH proton. The characteristic high frequency shift probably arises from the combined effects of the π-system, the electron-withdrawing atoms, and some interaction with the solvent. The effect of changing the substituents in the *m*- and *p*-substituted benzaldehyde sulfonohydrazones (**4**–**10**) was examined with particular reference to the position of the NH chemical shifts. The hydrazone (**11**) was excluded as the NH resonance signal was poorly defined, and (**12**) was also deleted due to poor solubility. Under conditions of constant concentration and the same solvent, there was a very good correlation coefficient ($r = 0.981$; standard deviation = 0.06), between the change in chemical shift, $\Delta\delta$ resulting from substitution, and the Hammett σ constant,[8] for which the regression line is:

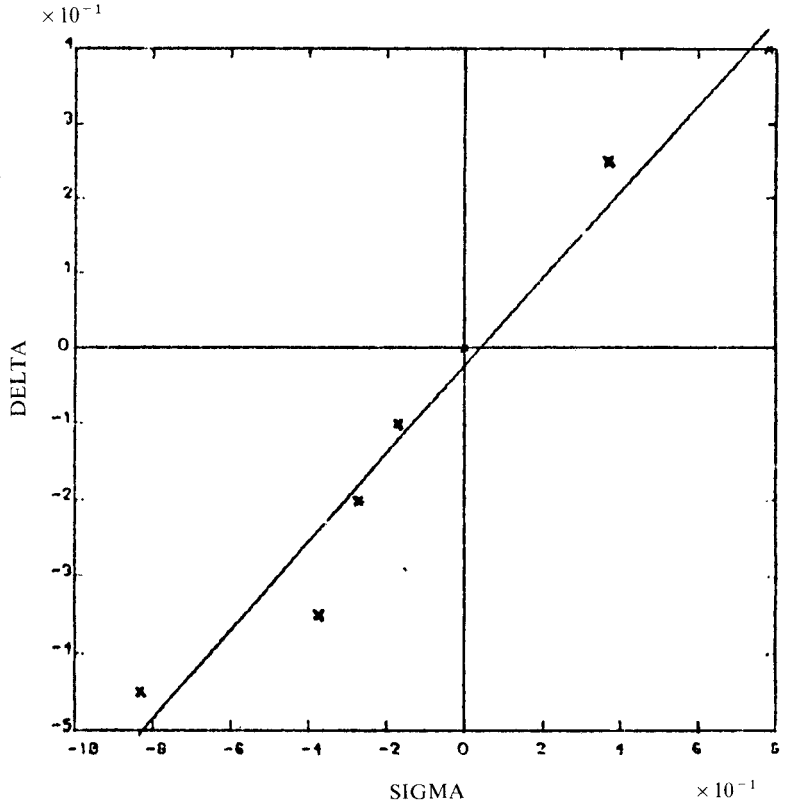
$$\Delta\delta = 0.58\sigma - 0.02$$

The Hammett plot is shown in Figure 1.

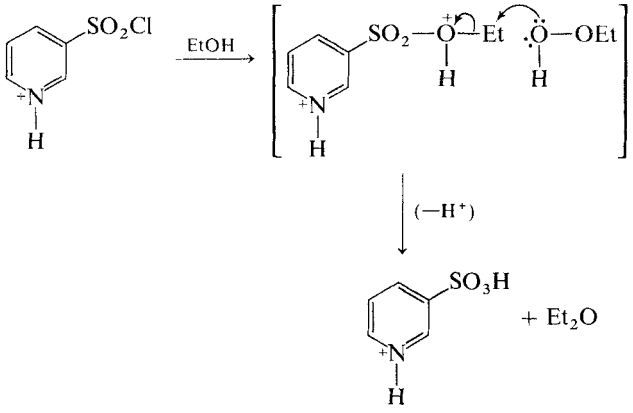
In addition to the conversion to the sulfonohydrazone derivatives, the hydrazide (**2**) was treated with methylisocyanate to give the corresponding N-methylsemicarbazide (**15**). Pyridine-3-sulfonyl azide (**16**) was prepared by the reaction of the sulfonyl chloride (**1**) with sodium azide as an oil, which was converted to the crystalline hydrochloride.

Quinoline-8-sulfonyl azide reacted with norbornene, but required prolonged boiling (10 h) in tetrahydrofuran to give the aziridine.[1] On the other hand, pyridine-3-sulfonyl azide (**16**) only required relatively mild conditions (boiling toluene 1 h) for the analogous reaction to form the aziridine derivative (**17**). The reduced reactivity shown by the quinoline sulfonyl azide probably arises from a steric *peri*-interaction between the hetero nitrogen atom and the azido group. The sulfonyl azide (**16**) also reacted readily with triphenylphosphine to give the iminophosphorane (**18**).

Treatment of quinoline-8-sulfonyl chloride with boiling ethanol has been shown[1] to give quinoline-8-sulfonic acid, which was attributed to the influence of neighbouring group participation by

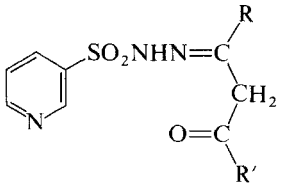


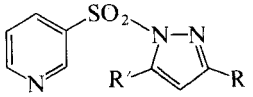
the *peri*-nitrogen atom. When pyridine-3-sulfonyl chloride (**1**) (as the hydrochloride) was similarly treated, the sulfonic acid (**3**) was also obtained. This reaction cannot however involve neighbouring group participation, but may be facilitated by the sulfonyl chloride (**1**) existing as the pyridinium salt:



(**3**)

Substituted pyrazoles have been prepared by the condensation of acylhydrazides[9–11] and sulfonohydrazides[12–14] with β-diketones; accordingly the reaction of pyridine-3-sulfonohydrazide (**2**) with a number of diketones was examined. The corresponding β-keto-sulfonohydrazones (**19–22**) were isolated, and in each case subsequent ring closure to give the pyrazoles (**19a–22a**) occurred.

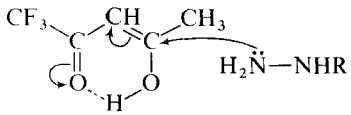




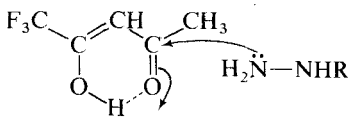
(**19**)–**22**)		(**19a**–**22a**)	
	R	*R′*	
(**19**)	CH_3	CH_3	(**19a**)
(**20**)	Ph	Ph	(**20a**)
(**21**)	CH_3	Ph	(**21a**)
(**22**)	CH_3	CF_3	(**22a**)
(**26**)	CH_3	OC_2H_5	

The structures of the hydrazones (**21**) and (**22**) were assigned on the basis of mass spectral data, which showed the presence of $PhC{\equiv}O^+$ and $CF_3C{\equiv}O^+$ respectively. The structure of the hydrazone (**21**) agrees with expectation, since steric and electronic factors combine to reduce the reactivity of the PhCO group as compared with the CH_3CO group in 1-phenylbutane-1,3-dione.

In 1,1,1-trifluoropentane-2,4-dione electronic factors would tend to make the CF_3CO group more reactive than the CH_3CO group; but this dione is known[15] to exist predominantly as the enol form (**23a**) or (**23b**), which could give the hydrazone (**22**) by a Michael-type addition, or direct addition respectively:

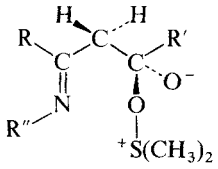


(**23a**)



(**23b**)

The proton resonance spectra of the hydrazones (**19–22**) always show a quartet at low frequency, which can be assigned to the CH_2 group. The non-equivalence and lack of enolisation of the CH_2 group may be attributed to solvation by the strongly nucleophilic dimethyl sulfoxide as indicated in structure (**24**):

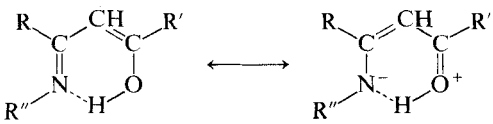


(**24**)

(R″ = pyridine-3-sulfonylimido)

Additional long-range effects may also contribute to the proton shieldings.

The absence of the carbonyl stretching absorption in the i.r. spectra of the hydrazones (**19, 21**) and the weakness of this absorption in the hydrazones (**20, 22**) suggests, that under the conditions of measurement, enolisation is complete or predominant. This would be expected as enolisation is favoured in non-polar media, and the enol is resonance stabilised (**25a**; **25b**):



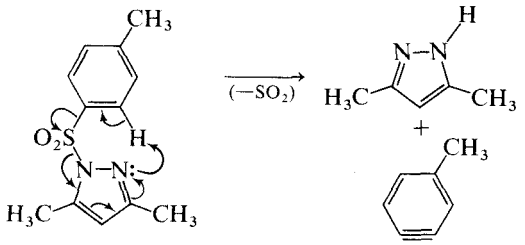
(**25a**) (**25b**)

(R″ = pyridine-3-sulfonylimido)

Condensation of pyridine-3-sulfonohydrazide (**2**) with ethyl acetoacetate gave the hydrazone (**26**) but all attempts to cyclise this compound to the corresponding pyrazole were unsuccessful.

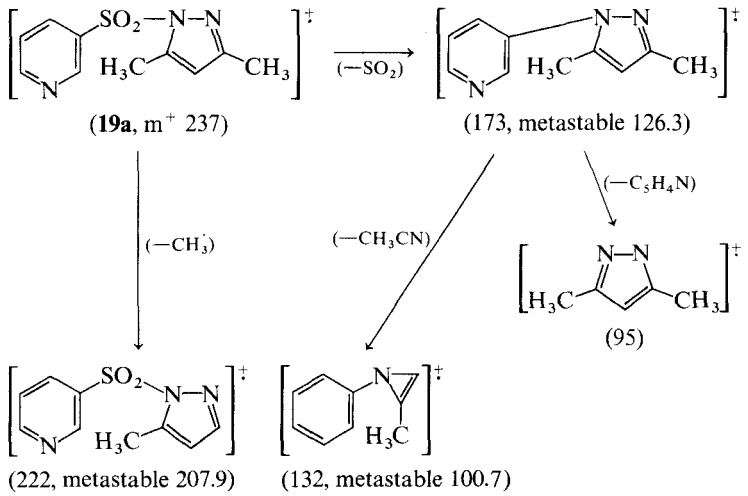
Mass spectra of the β-ketopyridine-3-sulfonohydrazones (**19–22**) indicated that elimination of water occurred with the formation of the corresponding pyridine-3-sulfonylpyrazoles (**19a–22a**). However, with the trifluoromethyl-(**22**) and ethoxy-(**26**) hydrazones, the predominant feature was loss of the trifluoromethyl or ethoxy groups.

Diphenylsulfone and sulfonylureas are known[16,17] to lose sulfur dioxide in the mass spectrometer. Nair[18] also observed that *p*-toluenesulfonylpyrazoles on heating (250°) eliminate sulfur dioxide with formation of the parent pyrazoles, for instance:



The existence of the benzyne intermediate was not proved, and we do not agree with Nair's proposed mechanism as the curly arrows would be expected to go from the pyrazole nitrogen atom to the toluenesulfonyl ring as depicted above, and not *vice-versa* (cf. Ref. 18).

We observed loss of sulfur dioxide in the mass spectra of the pyridine-3-sulfonyl pyrazoles; thus the dimethylpyrazole (**19a**) fragments as shown:



Here the net result loss of SO_2 does not involve the additional loss of the 3-pyridyl moiety attached to the pyrazole nucleus; in contrast *p*-toluenesulfonylpyrazoles suffer a different fragmentation involving a net loss of the toluene moiety from the pyrazole.[18] The difference in pyrolysis may arise from the presence of the heterocyclic pyridine nucleus. Thermolysis of allyl sulfones is an example of a similar process involving loss of sulfur dioxide.[19]

EXPERIMENTAL

I.r. spectra were recorded as potassium chloride discs on a Perkin Elmer 257 spectrophotometer. N.m.r. spectra were determined with a Varian HA 100 spectrometer, with tetramethylsilane as internal reference standard. Microanalyses were by Butterworth Microanalytical Laboratory, Teddington, England. Mass spectra were determined with an AEI MS 10 spectrometer.

Pyridine-3-sulfonyl chloride (**1**) *hydrochloride* The reaction of pyridine-3-sulfonic acid (**3**) with phosphorus pentachloride by the method of Reinhart[4] gave the sulfonyl chloride (**1**) which was isolated as the hydrochloride salt.

Pyridine-3-sulfonohydrazide (**2**) Pyridine-3-sulfonyl chloride (**1**) hydrochloride[4] (21.5 g) was added portionwise to a stirred solution of hydrazine hydrate (16.5 g; 3.3 equiv.) in methanol at 10°. After 1 h, the solid was filtered off, washed with water and dried over phosphorus pentoxide, to give *pyridine-3-sulfonohydrazide* (**2**) (12.0 g; 69%), m.p. 96–97° (lit.[5] 94°).

Benzaldehyde pyridine - 3 - sulfonohydrazone (**4**) Benzaldehyde (0.53 g) was added portionwise to the sulfonohydrazide (**2**) (0.86 g) in aqueous methanol at room temperature to give the benzaldehydesulfonohydrazone (**4**) as a white solid (0.7 g), m.p. 162–164° (Found: C, 55.5; H, 4.3; N, 16.5. $C_{12}H_{11}N_3O_2S$ requires: C, 55.2; H, 4.2; N, 16.1%). ν_{max} 1345, 1185 cm^{-1} (SO_2). N.m.r. ($(CD_3)_2$ SO, 0.04 M) δ 11.7, s (1H, SO_2NH),

9.0–7.3, m (9H, ArH, PyH), 7.9, s (1H, N = CH). The signal at δ 11.7 was removed by D_2O treatment.

The following pyridine-3-sulfonohydrazones were similarly prepared:

p-Nitrobenzaldehyde Pyridine-3-sulfonohydrazone (**5**) (95%), m.p. 128–129° (Found: C, 47.3; H, 3.4; N, 18.5. $C_{12}H_{10}N_4O_4S$ requires: C, 47.1; H, 3.3; N, 18.3%). ν_{max} 1350, 1180 cm^{-1} (SO_2). N.m.r. (($CD_3)_2$ SO, 0.04 M) δ 12.1, s (1H, SO_2NH), 9.1 – 7.5, m (8H, ArH, PyH), 8.11 s (1H, N = CH). The signal at δ 12.1 was removed by D_2O treatment.

m - Chlorobenzaldehyde Pyridine - 3 - sulfonohydrazone (**6**) (84%), m.p. 168–169° (Found: C, 48.9; H, 3.5; N, 13.9. $C_{12}H_{10}ClN_3O_2S$ requires: C, 48.7; H, 3.4; N, 14.2%). ν_{max} 1345, 1180 cm^{-1} (SO_2). N.m.r. (($CD_3)_2$ SO, 0.04 M) δ 11.9, s (1H, SO_2NH), 9.05–7.0, m (8H, ArH, PyH), 7.95, s (1H, N = CH). The signal at δ 11.9 was removed by D_2O treatment.

p-Methylbenzaldehyde Pyridine-3-sulfonohydrazone (**7**) (75%), m.p. 153–155° (Found: C, 57.1; H, 4.9; N, 15.2. $C_{13}H_{13}N_3O_2S$ requires: C, 56.7; H, 4.7; N, 15.3%). ν_{max} 1350, 1180 cm^{-1} (SO_2). N.m.r. (($CD_3)_2$ SO, 0.04 M) δ 11.6, s (1H, SO_2NH), 9.1–7.15, m (8H, ArH, PyH), 7.97, s (1H, N = CH), 2.3, s (3H, CH_3). The signal at δ 11.6 was removed by D_2O treatment.

p - Methoxybenzaldehyde Pyridine - 3 - sulfonohydrazone (**8**) (82%), m.p. 152–153° (Found: C, 53.9; H, 4.6; N, 14.6. $C_{13}H_{13}N_3O_3S$ requires: C, 53.6; H, 4.5; N, 14.4%). ν_{max} 1345, 1175 cm^{-1} (SO_2). N.m.r. (($CD_3)_2$ SO, 0.04 M) δ 11.5, s (1H, SO_2NH), 9.1 – 6.9, m (8H, ArH, PyH), 7.95, s (1H, N = CH), 3.8, s (3H, OCH_3). The signal at δ 11.5 was removed by D_2O treatment.

p - Hydroxybenzaldehyde Pyridine - 3 - sulfonohydrazone (**9**) (95%), m.p. 198–200° (Found: C, 52.1; H, 4.1; N, 15.0. $C_{12}H_{11}N_3O_3S$ requires: C, 52.0; H, 4.0; N, 15.2%). ν_{max} 1350, 1190 cm^{-1} (SO_2). N.m.r. (($CD_3)_2$ SO, 0.04 M) δ 11.35, s (1H, SO_2NH), 9.9, s (1H, OH), 9.0 – 6.7, m (8H, ArH, PyH), 7.82, s (1H, N = CH). The signal at δ 11.35 was removed by D_2O treatment.

p - N,N - Dimethylaminobenzaldehyde Pyridine - 3 - sulfonohydrazone (**10**) (86%), m.p. 170–171° (Found: C, 55.1; H, 5.3; N, 18.4. $C_{14}H_{16}N_4O_2S$ requires: C, 55.3; H, 5.3; N, 18.4%). ν_{max} 1345, 1175 cm^{-1} (SO_2). N.m.r. (($CD_3)_2$ SO, 0.04 M) δ 11.25, s (1H, SO_2NH), 9.03 – 6.6, m (8H, ArH, PyH), 7.84, s (1H, N = CH), 2.9, s (6H, NMe_2). The singlet at δ 11.25 was removed by D_2O treatment.

p - Chlorobenzaldehyde Pyridine - 3 - sulfonohydrazone (**11**) (67%), m.p. 171–172° (Found: C, 49.1; H, 3.4; N, 13.9. $C_{12}H_{10}ClN_3O_2S$ requires: C, 48.7; H, 3.4; N, 14.2%). ν_{max} 1345, 1180 cm^{-1} (SO_2). N.m.r. (($CD_3)_2$ SO, 0.04 M) δ 11.7, br s (1H, SO_2NH), 9.15 – 7.4, m (8H, ArH, PyH), 8.05, s (1H, N = CH). The signal at δ 11.65 was removed by D_2O treatment.

p - Phenylbenzaldehyde Pyridine - 3 - sulfonohydrazone (**12**) (88%) m.p. 170–171° (Found: C, 64.4; H, 4.7; N, 12.0. $C_{18}H_{15}N_3O_2S$ requires: C, 64.1; H, 4.4; N, 12.5%). ν_{max} 1345, 1175 cm^{-1}. N.m.r. (($CD_3)_2$ SO, 0.04 M) δ 11.8, s (1H, SO_2NH), 9.1 – 7.4, m (13H, ArH, PyH), 8.04, s (1H, N = CH). The signal at δ 11.8 was removed by D_2O treatment.

o-Nitrobenzaldehyde Pyridine-3-sulfonohydrazone (**13**) (81%), m.p. 149° (Found: C, 47.4; H, 3.2; N, 18.5. $C_{12}H_{10}N_4O_4S$ requires: C, 47.1; H, 3.3; N, 18.3%). ν_{max} 1350, 1180 cm^{-1} (SO_2). N.m.r. (($CD_3)_2$ SO, 0.04 M) δ 12.1, s (1H, SO_2NH), 9.1 – 7.4 (8H, ArH, PyH), 8.11, s (N = CH). The signal at δ 12.1 was removed by D_2O treatment.

Acetone Pyridine-3-sulfonohydrazone (**14**; R = R′ = Me) (75%), m.p. 163–165° (dec) (Found: C, 44.8; H, 5.2; N, 19.6 $C_8H_{11}N_3O_2S$ requires: C, 45.1; H, 5.2; N, 19.7%). N.m.r. ($CDCl_3$) δ 10.17, s (1H, NH), 8.95–7.50, m (4H, 4PyH), 1.75, s (6H, 2 × CH_3). The signal at δ 10.17 was removed by D_2O treatment.

Ethyl Methyl Ketone Pyridine-3-sulfonohydrazone (**14**; R = Et, R′ = Me) (85%), m.p. 128° (dec.) (Found: C, 47.4; H, 5.8; N, 18.6. $C_9H_{13}N_3O_2S$ requires: C, 47.6; H, 5.7; N, 18.5%). N.m.r. ($CDCl_3$) δ 10.15, s (1H, NH). 9.00 – 7.52, m (4H, 4PyH), 2.10, q (2H, CH_2), 1.75, s (3H, CH_3). 0.85, t (3H, CH_2CH_3). The signal at δ 10.15 was removed by D_2O treatment.

Acetophenone Pyridine-3-sulfonohydrazone (**14**; R = Ph, R′ = Me) (65%), m.p. 189° (dec.) (Found: C, 56.8; H, 4.4; N, 15.2. $C_{13}H_{13}N_3O_2S$ requires: C, 56.7; H, 4.7; N, 15.3%). N.m.r. (($CD_3)_2$ SO) δ 10.75, s (1H, NH), 9.05 – 7.25, m (9H, C_6H_5, 4PyH). The signal at δ 10.75 was removed by D_2O treatment.

Cyclohexanone Pyridine-3-sulfonohydrazone (**14**; R = R′ = $(CH_2)_5$) (96%), m.p. 144° (Found: C, 52.2; H, 6.3; N, 16.3. $C_{11}H_{15}N_3O_2S$ requires: C, 52.2; H, 6.0; N, 16.6%). ν_{max} 1340, 1170 cm^{-1} (SO_2). N.m.r. (($CD_3)_2$ SO, 0.04 M) δ 10.35, s (1H, SO_2NH), 9.0 – 7.55, m (4H, PyH), ≃2.2, m (4H, $CH_2\overset{\|}{C}CH_2$), 1.7 – 1.4, m (6H, $CH_2CH_2CH_2$). The signal at δ 10.35 was removed by D_2O treatment.

N(1) - Methyl N(3) - Pyridine - 3 - Sulfonyl Semicarbazide (**15**) Methylisocyanate (0.3 g) was added dropwise to a solution of pyridine-3-sulfonohydrazide (0.86 g) in acetonitrile (10 ml). After 45 min. at room temperature, the white crystals were filtered off and washed with cold acetonitrile to give the *N*(**1**)-*Methylsemicarbazide* (**15**) (0.85 g, 84%), m.p. 180° (dec.) (Found: C, 38.7; H, 4.7; N, 19.6. $C_7H_{10}N_3O_3S$ requires: C, 38.9; H, 4.6; N, 19.45%). ν_{max} 1360, 1180 (SO_2), 1680 (CONH) cm^{-1}. N.m.r. ($CDCl_3$) δ 9.70, s (1H, SO_2NH), 8.90 – 7.60, m (4PyH), 8.22, s (1H, NHCO), 6.35, q (1H, N*H*Me), 2.25, d (3H, CH_3). D_2O treatment removed the signals at δ 9.7, 8.22 and 6.35.

Pyridine-3-Sulfonyl Azide (**16**) Pyridine-3-sulfonyl chloride (**1**) hydrochloride (2.2 g) in water (10 ml) was added slowly to a cooled solution of sodium azide (0.65 g; 1 equiv.) in water (15 ml), and stirred for 1 h. Neutralisation with 5N hydrochloric acid and extraction with ether gave the sulfonyl azide (**16**), (1.5 g, 80%) as a pale yellow oil which was converted to the *hydrochloride* (1.8 g), m.p. 103–106° (Found: C, 27.2; H, 2.2; N, 25.3. $C_5H_5ClN_4O_2S$ requires: C, 27.2; H, 2.3; N, 25.4%). ν_{max} 2130 (N_3), 1385, 1170 cm^{-1} (SO_2).

Reactions of Pyridine-3-sulfonyl Azide (**16**) (i) *With norbornene*—A solution of pyridine-3-sulfonyl azide (1 g) and norbornene (0.5 g) in toluene (30 ml) was boiled for 1 h, when nitrogen (1 equiv.) had been evolved. After evaporation, the

residue was dissolved in ether, and treated with hydrogen chloride gas to give *N-(pyridine-3-sulfonyl) azatricyclo [3,2,1,0^{2,4}] octane* (**17**) *hydrochloride* (1 g; 65%), m.p. 92° (Found: C, 49.9; H, 5.4; N, 9.5. $C_{12}H_{15}ClN_2O_2S$ requires: C, 50.3; H, 5.3; N, 9.8%), ν_{max} 1370, 1180 cm^{-1} (SO_2) (ii) *With triphenylphosphine*—A solution of pyridine-3-sulfonyl azide (**16**) (1 g) and triphenylphosphine (1.4 g; 1 equiv.) in dry tetrahydrofuran (30 ml) was boiled until nitrogen (1 equiv.) had been evolved. The solvent was evaporated and the solid residue recrystallized from ethyl acetate to give *pyridine-3-sulfonyliminophosphorane* (1.5 g, 65%), m.p. 103–105°. (Found: C, 65.8; H, 4.7; N, 6.4. $C_{23}H_{19}N_2O_2PS$ requires: C, 66.0; H, 4.6; N, 6.7%). ν_{max}3070 (CH), 1440 (N = P), 1340, 1160 cm^{-1} (SO_2).

Preparation of the β - Ketopyridine - 3 - sulfonohydrazones (**19–22, 26**) Pyridine-3-sulfonohydrazide was reacted with the appropriate β-dicarbonyl compound (1 equiv.) in tetrahydrofuran at room temperature for 2 h. Evaporation of the solvent under reduced pressure and recrystallization of the residue afforded the β-ketosulfonohydrazone. By this procedure, 2,4-pentanedione gave the *dimethyl hydrazone* (**19**) (90% from tetrahydrofuran-toluene), m.p. 124–126° (Found: C, 46.8; H, 5.0; N, 16.6. $C_{10}H_{13}N_3O_3S$ requires: C, 47.05; H, 5.1; N, 16.5%). ν_{max} 3100 br (NH, OH), 1360, 1180 (SO_2) cm^{-1}. N.m.r. ($(CD_3)_2SO$) δ 9.20 – 9.02, m (1H, py – 2H), 8.90 – 8.80, m (1H, py – 6H), 8.32 – 8.22, m (1H, py – 4H), 8.0, br s (1H, NH), 7.76 – 7.52, m (1H, py – 5H), 2.82, q (2H, CH_2), 1.92, s (3H, CH_3CO), 1.82, s (3H, CH_3 – C = N). The signal at δ 8.0 was removed by D_2O treatment. Ms showed the molecular ion (M^+, 255) (5%), and other major ions at 237 (M – H_2O) (16%), 173(M – H_2O – SO_2) (85%), 143 (py – $3SO_2H$) (10%), 95 (100%), 78 (py) (69%), 44, 42, 33.

Phenylbutane-1,3-dione gave the *methylphenyl hydrazone* (**21**) (70% from toluene), m.p. 133–135°. (Found: C, 56.9; H, 4.6; N, 13.45. $C_{15}H_{15}N_3O_3S$ requires: C, 56.8; H, 4.8; N, 13.2%). ν_{max} 3100 br (NH, OH), 1360, 1180 (SO_2) cm^{-1}. N.m.r. ($(CD_3)_2SO$) δ 9.12 – 9.04, m (1H, Py – 2H), 8.90 – 8.80, m (1H, py – 6H), 8.35 – 8.20, m (py – 5H), 8.0, s (1H, NH), 7.90 – 7.79, m (py – 4H), 7.70 – 7.32, m (5H, C_6H_5), 3.02, q (2H, CH_2), 1.97, s (3H, CH_3). The signal at δ 8.0 was removed by D_2O treatment. Ms did not show the molecular ion (M^+, 317); major fragment ions were at 299 (M – H_2O, 15%), 234 (M – H_2O – SO_2, 32%), 158 (46%), 129 (41%), 105 (PhCO, 100%), 78 (py, 55%), 51 (42%).

1,3-Diphenylpropane-1,3-dione gave the *diphenyl hydrazone* (**20**) (80% from ethanol), m.p. 189–190° (Found: C, 63.3; H, 4.5; N, 10.9. $C_{20}H_{17}N_3O_3S$ requires: C, 63.3; H, 4.5; N, 11.1%). ν_{max} 3100 br (NH, OH), 1630 ω (C=O), 1360, 1180 (SO_2) cm^{-1}. N.m.r. ($(CD_3)_2SO$) δ 9.12 – 9.10, m (1H, py – 2H), 8.82 – 8.73, m (1H, py – 6H), 8.38 – 8.25, m (1H, py – 5H), 7.80 – 7.35, m (12H, 2 × C_6H_5, py – 4H, 1NH), 3.50, s (2H, CH_2).

1,1,1-Trifluoropentane-2,4-dione gave the *methyl trifluorohydrazone* (**22**) (95% from tetrahydrofuran-toluene), m.p. 204–206° (dec.) (Found: C, 38.8; H, 3.3; N, 13.8. $C_{10}H_{10}F_3N_3O_3S$ requires: C, 38.8; H, 3.3; N, 13.6%). ν_{max} 3070 br (OH), 2750 (NH), 1650 w (C=O), 1380, 1190 (SO_2) cm^{-1}. N.m.r. ($CDCl_3$ – $(CD_3)_2SO$) δ 9.10 – 9.06, m (1H, py – 2H), 8.92 – 8.82, m (1H, py – 6H), 8.40, s (1H, NH), 8.37 – 8.22, m (1H, py – 5H), 7.72 – 7.58, m (1H, py – 4H), 3.17, q (2H, CH_2, J 20 Hz), 1.98, s (3H, CH_3). The signal at δ 8.40 was removed after D_2O treatment. Ms showed the molecular ion (M^+, 309); other major ions were at 240 (M – CF_3, 40%), 176 (M – CF_3 – SO_2, 8%), 142 (8%), 98 (CF_3CO, 12%), 78 (100%), 69 (20%), 51 (45%).

Ethyl acetoacetate gave the *methyl ethoxy hydrazone* (**26**) (87% from tetrahydrofuran-toluene), m.p. 158–160° (Found: C, 46.5; H, 5.1; N, 14.3. $C_{11}H_{15}N_3O_4S$ requires: C, 46.3; H, 5.3; N, 14.3%). ν_{max} 2700 br (NH), 1740 (C=O), 1350, 1170 (SO_2) cm^{-1}. Ms showed the molecular ion (M^+ + 1, 286); other ions were at 240 (M – OEt, 10%), 212 (M – OEt – N_2, 8%), 159 ($PySO_3H$), 144 (30%), 126, 98 (92%), 78 (100%).

Preparation of the Pyrazoles (**19a–22a**) These were obtained by cyclisation (dehydration) of the β-ketopyridine-3-sulfonohydrazones (**19–22**). The dimethyl β-ketopyridine-3-sulfonohydrazone (**19**) (0.5 g) was boiled under reflux with ethyl acetate (25 ml) for 5 h. The suspension was filtered, the filtrate washed with water, and evaporated. Recrystallization of the residue from toluene gave the *dimethylpyrazole* (**19a**) (0.2 g), m.p. 102–104° (Found: C, 50.4; H, 4.9; N, 17.7. $C_{10}H_{11}N_3O_2S$ requires: C, 50.6; H, 4.7; N, 17.7%). ν_{max} 1350, 1170 (SO_2) cm^{-1}. N.m.r. ($CDCl_3$) δ 9.16 – 9.12, m (1H, py – 2H), 8.84 – 8.78, m (1H, py – 6H), 8.26 – 8.15, m (1H, py – 4H), 7.52 – 7.40, m (1H, py – 5H), 4.76, s (1H, CH), 1.96, s (3H, N – CH_3), 1.50, s (3H, C – CH_3). Ms showed the molecular ion (M^+, 237) and fragment ions at 222 (M – CH_3, 5%), 173 (M – SO_2, 65%), 172 (45%), 158 (10%), 143 (8%), 133 (15%), 95 (100%), 78 (80%), 51 (90%).

A suspension of the methyl phenyl hydrazone (**21**) (1 g) in chloroform (20 ml) was stirred with a solution of sodium methoxide for 1 h. The mixture was filtered and the filtrate evaporated to give the *methylphenylpyrazole* (**21a**) as a bright yellow solid (1 g, 95%), m.p. 183–185° (dec.) (Found: C, 59.9; H, 4.2; N, 13.8. $C_{15}H_{13}N_3O_2S$ requires: C, 60.2; H, 4.4; N, 14.0%). ν_{max}1350, 1185 (SO_2) cm^{-1}. N.m.r. ($CDCl_3$ – $(CD_3)_2SO$) δ 9.07 – 9.04, m (1H, py – 2H), 8.63 – 8.52, m (1H, py – 6H), 8.25 – 8.10, m (1H, py – 5H), 7.84 – 7.75, m (1H, py – 4H), 7.45 – 7.28, m (5H, C_6H_5), 5.49, s (1H, CH), 1.90, s (3H, CH_3).

The diphenyl hydrazone (**20**, 0.5 g) was boiled under reflux in chloroform (30 ml) with potassium carbonate (2 g) and anhydrous sodium sulfate (4 g) for 10 h. Evaporation and recrystallization (ethyl acetate–petroleum ether 40–60°) gave the *diphenylpyrazole* (**20a**) as colourless plates (0.35 g, 70%), m.p. 193–195° (Found: C, 66.1; H, 4.1; N, 11.5. $C_{20}H_{15}N_3O_2S$ requires: C, 66.5; H, 4.2; N, 11.6%). ν_{max} 1180 (SO_2) cm^{-1}. Ms showed the molecular ion (M^+, 361, 62%), 297 (M – SO_2, 14.7%), 219 (M – SO_2 – py, 90%), 191 (100%), 78 (52%), 64 (22%), 51 (41%).

The methyl trifluorohydrazone (**22**, 0.5 g) in ethyl acetate (30 ml) was boiled under reflux for 14 h with potassium carbonate (2 g) and anhydrous sodium sulfate (4 g). The mixture was filtered, and the filtrate concentrated to give the *methyl trifluoropyrazole* (**22a**, 62%), m.p. 193–196° (dec.) (Found: C, 41.0; H, 2.9; N, 14.1. $C_{10}H_8F_3N_3O_2S$ requires: C, 41.2; H, 2.8; N, 14.4%). ν_{max} 1150 (SO_2) cm^{-1}. N.m.r. ($(CD_3)_2SO$) δ 9.09 – 9.05, m (1H, py – 2H), 8.90 – 8.80, m (1H, py – 6H), 8.70 – 8.62, m (py – 5H), 8.40 – 8.05, br s (1H, NH), 7.57 – 7.44, m (1H, py – 4H), 5.00, s (1H, CH), 1.88, s (3H, CH_3).

Attempts to cyclise the Ethoxy Methyl Hydrazone (**26**) (i) The hydrazone (**26**) (0.5 g) was boiled with sodium ethoxide (1 equiv.) in chloroform for 4 h. Evaporation gave a coloured residue which after washing with water gave the starting hydrazone (0.3 g). The aqueous washings, by extraction ($CHCl_3$) gave no product. (ii) A suspension of the hydrazone (0.5 g) was boiled with sodium sulfate (4 g) and potassium

carbonate (2 g) in toluene (25 ml) for 24 h. Dilution with H_2O (50 ml) and extraction with ethyl acetate gave an uncrystallizable gum (0.4 g). (iii) Treatment of the hydrazone (0.5 g) with potassium carbonate (2 g) in water (20 ml) at 80° for $\frac{1}{2}$ h, and extraction with various solvents (e.g. $CHCl_3$, EtOAc, BuOH) afforded no product.

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