# A New Approach for Convenient One-pot Synthesis of 5-(1-Oxidopyridyl)- and 5-(1-Oxidoquinolyl)-2-alkylsulphonyl-1,3,4-thiadiazoles

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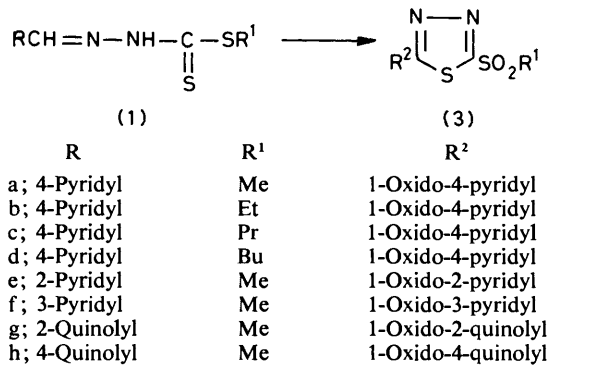
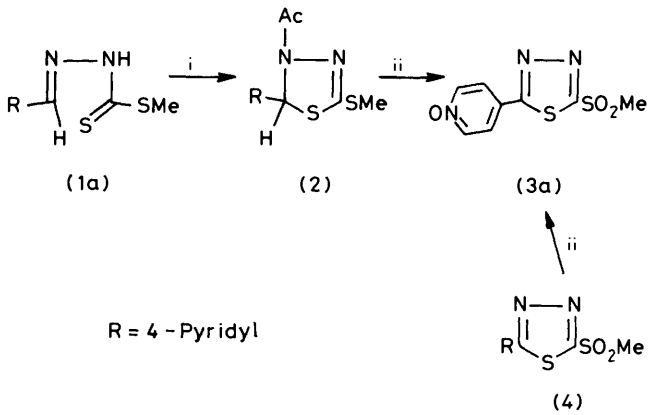
Acetylation of pyridine-4-carbaldehyde methylthio(thiocarbonyl)hydrazone (1a) with acetic anhydride gave 4-acetyl-2-methylthio-5-(4-pyridyl)-4,5-dihydro-1,3,4-thiadiazole (2). Oxidation of compound (2) with 30% hydrogen peroxide in acetic acid furnished 2-methylsulphonyl-5-(1-oxido-4-pyridyl)-1,3,4-thiadiazole (3a). 2-Alkylsulphonyl-1,3,4-thiadiazoles (3a—h) having 1-oxido-2-pyridyl, 1-oxido-3-3-pyridyl, 1-oxido-4-pyridyl, 1-oxido-2-quinolyl, and 1-oxido-4-quinolyl groups at the 5-position were obtained in good yields from the corresponding pyridine- (1a—f) and quinoline-carbaldehyde (1g) and (1h) alkylthio(thiocarbonyl)hydrazones by a one-pot synthesis. A reaction pathway from compound (2) to compound (3a) is also described.

In a previous paper,[1] we reported that acetylation of aldehyde methylthio(thiocarbonyl)hydrazones with acetic anhydride gave 5-(substituted phenyl) 4-acetyl-2-methylthio-$\Delta^2$-1,3,4-thiadiazolines (4-acetyl-2-methylthio-4,5-dihydro-1,3,4-thiadiazoles) in good yields, and that oxidation of these 1,3,4-thiadiazolines with 3 mol equiv. of potassium permanganate in acetic acid gave 5-(substituted phenyl) 4-acetyl-2-methylsulphonyl-$\Delta^2$-1,3,4-thiadiazoline 1,1-dioxides and 5-(substituted phenyl) 2-methylsulphonyl-1,3,4-thiadiazoles. However, in the case of 5-(substituted phenyl) 1,3,4-thiadiazolines having an electron-withdrawing group at the *para* position of the phenyl group, the only oxidized products obtained were 1,3,4-thiadiazole derivatives. On the basis of these findings, we have examined a new approach to 2-methylsulphonyl-5-(*N*-oxidoheteroaryl)-1,3,4-thiadiazoles (3a—h) from different pyridine- (1a—f) or quinoline-carbaldehyde (1g) and (1h) alkylthio(thiocarbonyl)hydrazones by a one-pot synthesis.

Acetylation of pyridine-4-carbaldehyde methylthio(thiocarbonyl)hydrazone (1a) [2] with acetic anhydride at 80 °C for 1 h gave 4-acetyl-2-methylthio-5-(4-pyridyl)-4,5-dihydro-1,3,4-thiadiazole (2) (Scheme 1). The chemical shift for the methine proton at $\delta_H$ 7.01 in the $^1$H n.m.r. spectrum and that for the sp$^3$ hybridised 5-carbon at $\delta_C$ 68.68 in the $^{13}$C n.m.r. spectrum of compound (2) are in good agreement with those of the C-5 proton and carbon of 4,5-dihydro-1,3,4-thiadiazole derivatives.[3]




**Scheme 1.**




**Scheme 2.** *Reagents:* i, $Ac_2O$; ii, 30% $H_2O_2$–$CH_3CO_2H$

Oxidation of 4,5-dihydro-1,3,4-thiadiazole (2) with an excess of 30% hydrogen peroxide in acetic acid at 90 °C for 2.5 h gave 2-methylsulphonyl-5-(1-oxido-4-pyridyl)-1,3,4-thiadiazole (3a) in 76% yield (Scheme 2). The structure of compound (3a) was established by direct comparison with an authentic sample obtained by *N*-oxidation [4] of the pyridine ring of 2-methylsulphonyl-5-(4-pyridyl)-1,3,4-thiadiazole (4) [5] with 30% hydrogen peroxide in acetic acid.

Compound (3a) was also prepared directly from the methylthio(thiocarbonyl)hydrazone (1a) without isolation of the 4,5-dihydro-1,3,4-thiadiazole (2) in a one-pot synthesis by acetylation followed by oxidation with 30% hydrogen peroxide in acetic acid. Similarly, the 2-alkylsulphonyl-5-(*N*-oxidoheteroaryl)-1,3,4-thiadiazoles (3b—h) were obtained from the corresponding pyridine- (1b—f) and quinoline-carbaldehyde (1g) and (1h) alkylthio(thiocarbonyl)hydrazones by a one-pot synthesis (Table).

It was observed by thin layer chromatography that the oxidation of the 4,5-dihydro-1,3,4-thiadiazole (2) into the 1,3,4-thiadiazole (3a) proceeds by way of several intermediates. This fact suggested that the reaction is a multistep procedure involving oxidation of the methylthio group, oxidation of the thiadiazole ring, and the formation of *N*-oxide.

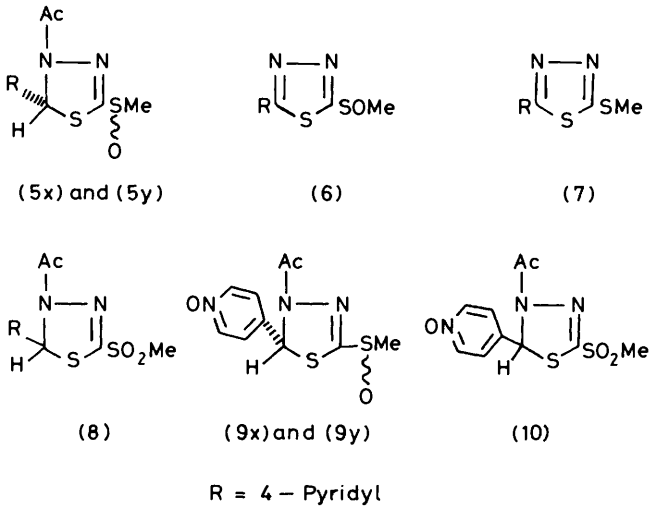
To clarify the reaction pathway from compound (2) to the 1,3,4-thiadiazole (3a), the isolation and conversion of each intermediate into the next was undertaken by changing the reaction conditions.

Treatment of compound (2) with 30% hydrogen peroxide (1 mol equiv.) in acetic acid at 85 °C for 1 h gave a diastereoisomeric mixture of the 4-acetyl-2-methylsulphinyl-5-(4-pyridyl)-4,5-dihydro-1,3,4-thiadiazoles (5x) and (5y) in 87%

**Table.** 2-Alkylsulphonyl-5-(*N*-oxidoheteroaryl)-1,3,4-thiadiazoles

| Compd. | M.p. (°C) | Yield (%) | Formula | Found (%) (Required) C | H | N | $\nu_{max.}$ (KBr) ($cm^{-1}$) $SO_2$ | N–O | *m/z* $M^+$ |
|---|---|---|---|---|---|---|---|---|---|
| (3b) | 189—190 | 56 | $C_9H_9N_3O_3S_2$ | 39.8 (39.8) | 3.0 (3.3) | 15.3 (15.5) | 1 150, 1 335 | 1 270 | 271 |
| (3c) | 181—182 | 61 | $C_{10}H_{11}N_3O_3S_2$ | 42.1 (42.1) | 3.6 (3.9) | 14.8 (14.7) | 1 150, 1 340 | 1 275 | 285 |
| (3d) | 168—169 | 54 | $C_{11}H_{13}N_3O_3S_2$ | 44.3 (44.1) | 4.3 (4.4) | 13.9 (14.0) | 1 150, 1 335 | 1 280 | 299 |
| (3e) | 199—200 | 70 | $C_8H_7N_3O_3S_2$ | 37.4 (37.4) | 2.8 (2.7) | 16.6 (16.3) | 1 160, 1 330 | 1 250 | 257 |
| (3f) | 223—224 * | 73 | $C_8H_7N_3O_3S_2$ | 37.6 (37.4) | 2.7 (2.7) | 16.4 (16.3) | 1 160, 1 320 | 1 270 | 257 |
| (3g) | 252—253 * | 54 | $C_{12}H_9N_3O_3S_2$ | 47.0 (46.9) | 2.7 (3.0) | 13.7 (13.7) | 1 160, 1 325 | 1 245 | 307 |
| (3h) | 205—208 * | 71 | $C_{12}H_9N_3O_3S_2$ | 46.7 (46.9) | 3.0 (3.0) | 13.7 (13.7) | 1 150, 1 320 | 1 220 | 307 |

* With decomposition.




yield along with 2-methylsulphinyl-5-(4-pyridyl)-1,3,4-thiadiazole (6) (7%). Repeated attempts to separate the diastereoisomers (5x) and (5y) by column chromatography were unsuccessful, although the ratio 3 : 2 was determined by integration of the resulting absorptions of the respective protons of compound (5x) and (5y) on the basis of $^1H$ n.m.r. spectroscopy.

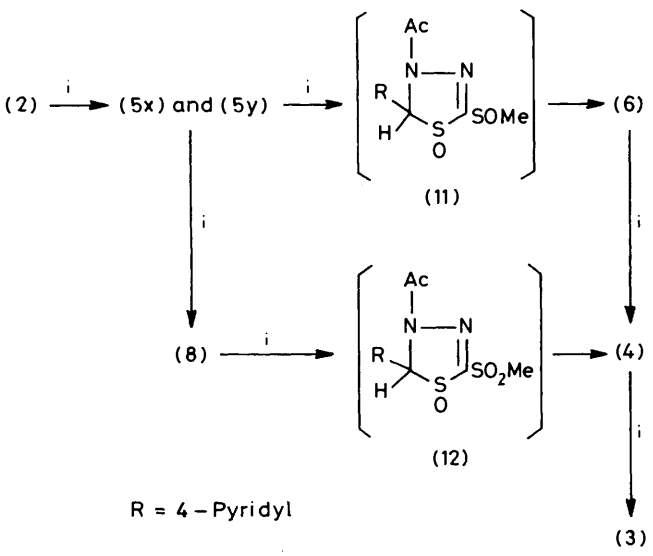
The structures of compounds (5x) and (5y) were determined by i.r., mass, and $^1H$ and $^{13}C$ n.m.r. spectroscopy. A strong peak at 1 065 $cm^{-1}$ is due to a sulphinyl group. The $^1H$ n.m.r. spectrum of the mixture (5x) and (5y) showed 2-methylsulphinyl protons at $\delta_H$ 2.94 and 2.98 as a singlet and 5-H protons at $\delta_H$ 7.09 and 7.05. The $^{13}C$ n.m.r. spectrum of the diastereoisomers showed the $sp^3$ hybridised 5-carbons at $\delta_C$ 69.90 and 69.09. The structure of compound (6) was assigned on the basis of its spectral data and confirmed by direct comparison with an authentic sample obtained by *S*-oxidation of 2-methylthio-5-(4-pyridyl)-1,3,4-thiadiazole (7) [5] with *m*-chloroperbenzoic acid.

Oxidation of the diastereoisomeric mixture (5x) and (5y) with 30% hydrogen peroxide (1 mol equiv.) in acetic acid at room temperature under stirring for 38 h gave 2-methylsulphinyl-5-(4-pyridyl)-1,3,4-thiadiazole (6) (16%), 4-acetyl-2-methylsulphonyl-5-(4-pyridyl)-4,5-dihydro-1,3,4-thiadiazole (8) (5%), and 2-methylsulphonyl-5-(4-pyridyl)-1,3,4-thiadiazole [5] (4) (3%), along with a small amount of a diastereoisomeric mixture of 4-acetyl-2-methylsulphinyl-5-(1-oxido-4-pyridyl)-4,5-dihydro-1,3,4-thiadiazole (9x) and (9y) (3%); the mixture (5x) and (5y) (48%) was unchanged.

The structure of compound (8) was determined from its spectral data. The mass spectrum showed a molecular ion at *m/z* 285 and peaks at *m/z* 242 ($M^+ - COCH_3$) and 206 ($M^+ - SO_2CH_3$). The i.r. spectrum showed sulphonyl absorptions at 1 340 and 1 160 $cm^{-1}$ and the $^{13}C$ and $^1H$ n.m.r. spectra both indicated the presence of the $sp^3$ hybridised 5-carbon ($\delta_C$ 71.80) and 5-methine proton ($\delta_H$ 7.14). The structures of the diastereoisomers (9x) and (9y) were assigned by their mass, i.r., and $^1H$ and $^{13}C$ n.m.r. spectra. The mass spectrum showed a molecular ion at *m/z* 285, and fragment ions at *m/z* 269 ($M^+ - O$) and 253 [$M^+ - (O + O)$], showing the presence of *N*-oxide and methylsulphinyl groups in the molecule. The i.r. spectrum showed peaks at 1 060 $cm^{-1}$ due to a sulphinyl group and 1 260 $cm^{-1}$ due to the pyridine *N*-oxide. The $^1H$ n.m.r. spectrum of the diastereoisomeric mixture (9x) and (9y) showed sulphinyl methyl protons at the same chemical shift, $\delta_H$ 2.97, and 5-methine protons at $\delta_H$ 7.10 and 7.06 as in the case of compounds (5x) and (5y). Aromatic proton signals at $\delta_H$ 8.18—8.25 agreed with those of the α protons of pyridine *N*-oxide.[6] The $^{13}C$ n.m.r. spectrum of the diastereoisomers showed the $sp^3$ hybridised 5-carbons at $\delta_C$ 68.62 and 69.23, and the signals of the α carbons in the pyridine *N*-oxide moieties at $\delta_C$ 139.54 and 139.46, with an upfield shift of *ca.* 1 p.p.m. from those of the α carbons of the pyridine rings in compounds (5x) and (5y), in good agreement with the α carbon shift reported for pyridine *N*-oxide.[7]

Oxidation of compound (6) with 30% hydrogen peroxide (1 mol equiv.) in acetic acid gave the 2-methylsulphonyl derivative (4) as the major product in 50% yield along with a minor product, compound (3a), in 16% yield.

Oxidation of compound (8) with 30% hydrogen peroxide in acetic acid at room temperature for 48 h gave compound (4) (24%), 4-acetyl-2-methylsulphonyl-5-(1-oxido-4-pyridyl)-4,5-dihydro-1,3,4-thiadiazole (10) (10%) along with the starting material (8) (59%). The structure of compound (10) was assigned from its spectral data. The mass spectrum showed a molecular ion at *m/z* 301 and a fragment ion at 285 ($M^+ - O$) due to the presence of a pyridine *N*-oxide group. The i.r. spectrum showed characteristic absorption bands at 1 260 (N–O) and 1 325 and 1 155 $cm^{-1}$ ($SO_2$). The $^1H$ n.m.r. spec-




**Scheme 3.** *Reagents:* i, 30% $H_2O_2$–$CH_3CO_2H$

trum showed a 5-methine proton at $\delta_H$ 7.13, and the α proton in the pyridine *N*-oxide moiety at $\delta_H$ 8.22. The $^{13}C$ n.m.r. spectrum showed the $sp^3$ hybridised 5-carbon at $\delta_C$ 71.07, and the α carbon signal of the pyridine *N*-oxide moiety in compound (10) at $\delta_C$ 139.75 as in the case of compounds (9x) and (9y) described above.

It has been reported that oxidation of bis(2-pyridylmethyl) sulphide with *m*-chloroperbenzoic acid gave bis(2-pyridylmethyl) sulphone without competitive *N*-oxidation,[8] while treatment of diphenyl sulphoxide with pyridine *N*-oxide gave diphenyl sulphone and pyridine;[9] also the rates of oxidation of sulphoxides to sulphones are slower than those for the oxidation of the related sulphides when peracetic acid is used as oxidant.[10] Previously, we have reported that oxidation of $\Delta^2$-1,3,4-thiadiazoline derivatives with *m*-chloroperbenzoic acid gave unstable $\Delta^2$-1,3,4-thiadiazoline 1-oxides.[1,11]

From our results and these facts, it was concluded that the reaction proceeds from compound (2) to compound (3a) by way of the intermediates (5), (11), (6), and (4), successively; compounds (5x) and (5y) were first oxidized to an unstable intermediate, 4-acetyl-2-methylsulphinyl-5-(4-pyridyl)-4,5-dihydro-1,3,4-thiadiazole 1-oxide (11) (Scheme 3), which was easily converted into the 2-methylsulphinyl-1,3,4-thiadiazole (6) with the help of the electron-withdrawing effect of the pyridine ring, and then oxidized to the methylsulphonyl-1,3,4-thiadiazole (4). A small amount of 4-acetyl-2-methylsulphonyl-5-(4-pyridyl)-4,5-dihydro-1,3,4-thiadiazole (8) was obtained as a minor product from the starting sulphoxides (5x) and (5y) and then easily oxidized to compound (4) *via* an unstable intermediate, 4-acetyl-2-methylsulphonyl-5-(4-pyridyl)-4,5-dihydro-1,3,4-thiadiazole 1-oxide (12).

## Experimental

M.p.s were determined by the capillary method and are uncorrected. I.r. spectra were recorded on a Hitachi 215 spectrometer. $^1H$ N.m.r. spectra were recorded on a JEOL PS-100 spectrometer using tetramethylsilane as internal standard, and $^{13}C$ n.m.r. spectra on a JEOL FX-200 spectrometer. Mass spectra were measured with a JEOL D-300 instrument. For column chromatography, a 1 : 1 mixture of Merk Kieselgel (70—230 mesh) and Mallinckrodt silicic acid (100 mesh) was employed. Oxidation reactions were carried out under argon. Ether refers to diethyl ether.

*Acetylation of Pyridine-4-carbaldehyde Methylthio(thiocarbonyl)hydrazone* (1a) *with Acetic Anhydride.*—A mixture of compound (1a), m.p. 176—178 °C (decomp.) [lit.,[2] 203 °C (decomp.)] (2.0 g, 9.48 mmol) and acetic anhydride (38 ml) was heated at 80 °C for 1 h, and the solution was then evaporated to dryness under reduced pressure. The resulting solid was crystallised from methanol–ether to give *4-acetyl-2-methylthio-5-(4-pyridyl)-4,5-dihydro-1,3,4-thiadiazole* (2) (1.90 g, 79%), m.p. 128—130 °C; $\nu_{max.}$ (KBr) 1 665 $cm^{-1}$ (C=O); $\delta_H$ ($CDCl_3$) 2.32 (3 H, s, $COCH_3$), 2.58 (3 H, s, $SOCH_3$), 7.01 (1 H, s, 5-H), 7.19 (2 H, dd, ArH), and 8.58 (2 H, dd, ArH); $\delta_C$ ($CDCl_3$) 22.10 ($COCH_3$), 15.68 ($SCH_3$), 68.65 (C-5), 120.30 (Ar C-3′, -5′), 148.16 (Ar C-4′), 150.26 (Ar C-2′, -6′), 151.25 (C-2), and 168.36 p.p.m. ($COCH_3$); *m/z* 253 ($M^+$), 210 ($M^+ - COCH_3$), 163 ($M^+ - COCH_3 - SCH_3$) (Found: C, 47.5; H, 4.4; N, 16.8. $C_{10}H_{11}N_3OS_2$ requires C, 47.4; H, 4.4; N, 16.6%).

*2-Methylsulphonyl-5-(1-oxido-4-pyridyl)-1,3,4-thiadiazole* (3a).—(*a*) *Oxidation of compound* (2) *with hydrogen peroxide in acetic acid.* To a stirred mixture of 30% hydrogen peroxide (0.9 g, 7.94 mmol) and acetic acid (2 ml), a solution of compound (2) (0.2 g, 0.79 mmol) in acetic acid (2 ml) was added dropwise and the reaction mixture was heated at 90 °C for 2.5 h. The reaction mixture was evaporated under reduced pressure, and the resulting residue was crystallised from methanol to give *2-methylsulphonyl-5-(1-oxido-4-pyridyl)-1,3,4-thiadiazole* (3a) (0.154 g, 76%), m.p. 219—220 °C (Found: C, 37.2; H, 2.6; N, 16.6. $C_8H_7N_3O_3S_2$ requires C, 37.4; H, 2.7; N, 16.3%); $\nu_{max.}$ (KBr) 1 330, 1 155 ($SO_2$), and 1 280 $cm^{-1}$ (NO); $\delta_H$ [$(CD_3)_2SO$] 3.64 (3 H, s, $SO_2CH_3$), 8.10 (2 H, dd, ArH), and 8.40 (2 H, dd, ArH); *m/z* 257 ($M^+$), 241 ($M^+ - O$), 178 ($M^+ - SO_2CH_3$).

(*b*) *N-Oxidation of 2-methylsulphonyl-5-(4-pyridyl)-1,3,4-thiadiazole.*[4] To a stirred solution of compound (4) [4] (0.048 g, 0.2 mmol) in acetic acid (1.5 ml), 30% hydrogen peroxide (0.025 g, 0.22 mmol) was added and the reaction mixture was heated at 70 °C for 1 h. The mixture was evaporated under reduced pressure and the residue was crystallised from methanol to give compound (3a) (0.04 g, 78%) as yellowish crystals, m.p. 219—220 °C. This product was found to be identical in all respects with a sample of compound (3a) which was prepared by direct oxidation of compound (2).

*One-pot Synthesis of 2-Methylsulphonyl-5-(1-oxido-4-pyridyl)-1,3,4-thiadiazole* (3a).—A mixture of compound (1a) (1.0 g, 4.74 mmol) and acetic anhydride (15 ml) was heated at 90 °C for 1 h. After the reaction mixture had been cooled, water (4.5 ml) was added, followed by 30% hydrogen peroxide (6.6 g, 58.2 mmol) under cooling. The mixture was heated at 90 °C for 2 h. Usual work-up as described in the above method gave yellowish crystals of compound (3a) (0.96 g, 79%), m.p. 219—220 °C.

*Pyridine- and Quinoline-carbaldehyde Alkylthio(thiocarbonyl)hydrazones* (1b—h).—Compound (1e), m.p. 177—178 °C (decomp.) (lit.,[2] 180—182 °C), compound (1f), m.p. 197—198 °C (decomp.) [lit.,[2] 197.5 °C (decomp.)], and compound (1 g), m.p. 193—195 °C (decomp.) [lit.,[2] 192—194 °C (decomp.)] were prepared by the literature method.[2] Compounds (1b), (1c), (1d), and (1h) were prepared by a method similar to that reported previously [1] from the corresponding aldehydes and alkyldithiocarbazates. *Pyridine-4-carbaldehyde ethylthio(thiocarbonyl)hydrazone* (1b) (88%), m.p. 159—160 °C (benzene) (Found: C, 48.0; H, 4.8; N, 18.8. $C_9H_{11}N_3S_2$ requires C, 48.0; H, 4.9; N, 18.7%).

*Pyridine-4-carbaldehyde propylthio(thiocarbonyl)hydrazone* (1c) (80%), m.p. 133—135 °C (benzene–ether) (Found: C,

50.1; H, 5.3; N, 17.3. $C_{10}H_{13}N_3S_2$ requires C, 50.2; H, 5.5; N, 17.6%).

*Pyridine-4-carbaldehyde butylthio(thiocarbonyl)hydrazone* (1d) (83%), m.p. 131—133 °C (light petroleum–ether) (Found: C, 51.9; H, 5.9; N, 16.7. $C_{11}H_{15}N_3S_2$ requires C, 52.1; H, 6.0; N, 16.6%).

*Quinoline-4-carbaldehyde methylthio(thiocarbonyl)hydrazone* (1h) (76%) m.p. 176—178 °C (ethanol) (Found: C, 55.1; H, 4.1; N, 15.9. $C_{12}H_{11}N_3S_2$ requires C, 55.2; H, 4.2; N, 16.1%).

*One-pot Synthesis of 2-Alkylsulphonyl-5-(N-oxidoheteroaryl)-1,3,4-thiadiazoles* (3b—h).—2-Alkylsulphonyl-5-substituted 1,3,4-thiadiazoles (3b—h) were prepared in a similar manner to that described for compound (3a). Yields, m.p.s, analytical, and i.r. spectral data for compounds (3b—h) are reported in the Table.

*Oxidation of Compound* (2) *with Hydrogen Peroxide in Acetic Acid.*—A mixture of 30% hydrogen peroxide (1.24 g, 10.9 mmol) and acetic acid (7 ml) was stirred at room temperature for 1 h. To the mixture, a solution of compound (2) (2.53 g, 10 mmol) in acetic acid (13 ml) was added, and the reaction mixture was gradually heated up to 85 °C. After being stirred at 85 °C for 1 h, the mixture was evaporated under reduced pressure. Column chromatography of the residue on silica gel (chloroform–methanol, 20 : 1 v/v) gave two fractions. Evaporation of the first fraction gave a solid which was crystallised from ethanol to give crystals of 2-*methylsulphinyl-5-(4-pyridyl)-1,3,4-thiadiazole* (6) (0.15 g, 7%), m.p. 154—155 °C (Found: C, 42.3; H, 2.8; N, 18.9. $C_8H_7N_3OS_2$ requires C, 42.7; H, 3.1; N, 18.7%); $\nu_{max.}$ (KBr) 1 070 $cm^{-1}$ (SO); $\delta_H$ ($CDCl_3$) 3.20 (3 H, s, $SOCH_3$), 7.86 (2 H, dd, ArH), and 8.83 (2 H, dd, ArH); *m/z* 225 ($M^+$), 209 ($M^+$ − O).

Evaporation of the second fraction gave a diastereoisomeric mixture of *4-acetyl-2-methylsulphinyl-5-(4-pyridyl)-4,5-dihydro-1,3,4-thiadiazoles* (5x) and (5y) as a yellowish oil (2.35 g, 87%) (Found: $M^+$, 269.0299. $C_{10}H_{11}N_3O_2S_2$ requires $M^+$, 269.0292); *m/z* 269 ($M^+$), 226 ($M^+$ − $COCH_3$), and 206 ($M^+$ − $SOCH_3$); $\nu_{max.}$ (film) 1 680 (C=O) and 1 065 $cm^{-1}$ (SO).

The major diastereoisomer showed $\delta_H$ ($CDCl_3$) 2.36 (3 H, s, $COCH_3$), 2.94 (3 H, s, $SOCH_3$), 7.09 (1 H, s, 5-H), 7.15—7.33 (2 H, m, ArH), and 8.58—8.64 (2 H, m, ArH); $\delta_C$ ($CDCl_3$) 22.13 ($COCH_3$), 41.70 ($SOCH_3$), 69.90 (C-5),120.15 (Ar C-3′, -5′), 147.49 (Ar C-4′), 150.58 (Ar C-2′, -6′), 160.19 (C-2), and 169.76 p.p.m. ($COCH_3$). The minor diastereoisomer showed $\delta_H$ ($CDCl_3$) 2.34 (3 H, s, $COCH_3$), 2.98 (3 H, s, $SOCH_3$), 7.05 (1 H, s, 5-H), 7.15—7.33 (2 H, m, ArH), and 8.58—8.64 (2 H, m, ArH), $\delta_C$ ($CDCl_3$) 22.22 ($COCH_3$), 41.05 ($SOCH_3$), 69.09 (C-5), 120.53 (Ar C-3′, -5′), 147.84 (Ar C-4′), 150.49 (Ar C-2′, -6′), 160.01 (C-2), and 169.59 p.p.m. ($COCH_3$).

*Oxidation of the Diastereoisomeric Mixture* (5x) *and* (5y) *with Hydrogen Peroxide in Acetic Acid.*—A mixture of 30% hydrogen peroxide (0.885 g, 7.8 mmol) and acetic acid (4 ml) was stirred at room temperature for 1 h. To the mixture, a solution of a diastereoisomeric mixture of (5x) and (5y) (2.1 g, 7.8 mmol) in acetic acid (8 ml) was added. After being stirred at room temperature for 38 h, the reaction mixture was evaporated under reduced pressure, and the residue was chromatographed on a silica gel column (chloroform–methanol, 100 : 1 v/v). Evaporation of the first fraction gave 2-methylsulphonyl-5-(4-pyridyl)-1,3,4-thiadiazole (4) [6] (0.057 g, 3%), m.p. 203—204 °C, $\nu_{max.}$ (KBr) 1 325 and 1 155 $cm^{-1}$ ($SO_2$). Evaporation of the second fraction gave a solid, which was a mixture of two components. Column chromatography on silica gel using acetone as eluant afforded 2-methylsulphinyl-5-(4-pyridyl)-1,3,4-thiadiazole (6) (0.281 g, 16%), m.p. 154—155 °C and *4-acetyl-2-methylsulphonyl-5-(4-pyridyl)-4,5-dihydro-1,3,4-thiadiazole* (8) (0.111 g, 5%) as a syrup (Found: $M^+$, 285.0252. $C_{10}H_{11}N_3O_3S_2$ requires $M^+$, 285.0241); *m/z* 285 ($M^+$), 242 ($M^+$ − $COCH_3$), and 206 ($M^+$ − $SO_2CH_3$); $\nu_{max.}$ (film) 1 690 (C=O), 1 340, and 1 160 $cm^{-1}$ ($SO_2$); $\delta_H$ ($CDCl_3$) 2.39 (3 H, s, $COCH_3$), 3.31 (3 H, s, $SO_2CH_3$), 7.14 (1 H, s, 5-H), 7.27 (2 H, dd, ArH), and 8.69 (2 H, d, ArH); $\delta_C$ ($CDCl_3$) 22.19 ($COCH_3$), 42.28 ($SO_2CH_3$), 71.80 (C-5), 120.45 (Ar C-3′, -5′), 146.96 (Ar C-4′), 150.76. 150.84 (Ar C-2′, -6′), 151.95 (C-2), and 169.82 p.p.m. ($COCH_3$).

Evaporation of the third fraction gave the starting material (5x) and (5y) (1.01 g). Evaporation of the fourth fraction gave a yellowish oil which was identified as the diastereoisomeric mixture of *4-acetyl-2-methylsulphinyl-5-(1-oxido-4-pyridyl)-4,5-dihydro-1,3,4-thiadiazole* (9x) and (9y) (0.067 g, 3%) (Found: $M^+$, 285.0243. $C_{10}H_{11}N_3O_3S_2$ requires $M^+$, 285.0241); *m/z* 285 ($M^+$), 269 ($M^+$ − O), and 253 [$M^+$ − (O + O)]; $\nu_{max.}$ (film) 1 680 (C=O), 1 260 (N−O), and 1 060 $cm^{-1}$ (SO). The major diastereoisomer showed $\delta_H$ ($CDCl_3$) 2.33 (3 H, s, $COCH_3$), 2.97 (3 H, s, $SOCH_3$), 7.10 (1 H, s, 5-H), 7.24—7.37 (2 H, m, ArH), and 8.18—8.25 (2 H, m, ArH); $\delta_C$ ($CDCl_3$) 22.19 ($COCH_3$), 41.58 ($SOCH_3$), 68.62 (C-5), 123.89 (Ar C-3′, -5′), 137.76 (Ar C-4′), 139.54 (Ar C-2′, -6′), 160.04 (C-2), and 169.97 p.p.m. ($COCH_3$). The minor diastereoisomer showed $\delta_H$ ($CDCl_3$) 2.31 (3 H, s, $COCH_3$), 2.97 (3 H, s, $SOCH_3$), 7.06 (1 H, s, 5-H), 7.24—7.37 (2 H, m, ArH), and 8.18—8.25 (2 H, m, ArH); $\delta_C$ ($CDCl_3$) 22.28 ($COCH_3$), 40.97 ($SOCH_3$), 69.23 (C-5), 124.21 (Ar C-3′, -5′), 137.50 (Ar C-4′), 139.46 (Ar C-2′, -6′), 160.04 (C-2), and 169.76 p.p.m. ($COCH_3$).

*Oxidation of 2-Methylthio-5-(4-pyridyl)-1,3,4-thiadiazole* (7) *with m-Chloroperbenzoic Acid.*—To a stirred solution of compound (7) [5] (0.337 g, 1.6 mmol) in chloroform (3 ml), a solution of 80% *m*-chloroperbenzoic acid (0.348 g, 1.6 mmol) in chloroform (4 ml) was added at 0 °C. After being stirred at 0 °C for 2.5 h, the mixture was neutralised with 5% aqueous sodium hydrogen carbonate and then extracted with chloroform (3 × 50 ml). The combined extracts were dried ($Na_2SO_4$). Evaporation of the solvent under reduced pressure gave a solid which was crystallised from ethanol to give needles of 2-methylsulphinyl-5-(4-pyridyl)-1,3,4-thiadiazole (6) (0.281 g, 77%), m.p. 154—155 °C. A sample of compound (6), obtained by oxidation of compound (2) with hydrogen peroxide in acetic acid, was identical in all respects with that prepared by the method described above.

*Oxidation of Compound* (6) *with Hydrogen Peroxide in Acetic Acid.*—A mixture of 30% hydrogen peroxide (0.056 g, 0.49 mmol) and acetic acid (1 ml) was stirred at room temperature for 1 h. To the mixture, a solution of compound (6) (0.112 g, 0.49 mmol) in acetic acid (1 ml) was added, and the reaction mixture was gradually heated up to 50 °C. After being stirred at 50 °C for 5 h, the mixture was evaporated under reduced pressure. Column chromatography of the resulting residue on silica gel (chloroform–methanol, 20 : 1 v/v) afforded 2-methylsulphonyl-5-(4-pyridyl)-1,3,4-thiadiazole (4) (0.06 g, 50%), m.p. 203—204 °C (lit.,[5] 202—203 °C), $\nu_{max.}$ (KBr) 1 325 and 1 155 $cm^{-1}$ ($SO_2$); *m/z* 241 ($M^+$), together with the minor product (3a) (0.02 g, 16%) and the starting material (7) (0.02 g).

*Oxidation of Compound* (8) *with Hydrogen Peroxide in Acetic Acid.*—A mixture of 30% hydrogen peroxide (0.06 g, 0.53 mmol) and acetic acid (0.5 ml) was stirred at room temperature for 2 h. To the mixture, a solution of compound (8) (0.15 g, 0.52 mmol) in acetic acid (1.5 ml) was added. After being stirred at room temperature for 48 h, the reaction mix-

ture was evaporated under reduced pressure. Column chromatography of the residue on silica gel (chloroform–methanol, 80 : 1 v/v) gave three fractions. Evaporation of the first fraction gave a solid which was crystallised from ethanol to give crystals of 2-methylsulphonyl-5-(4-pyridyl)-1,3,4-thiadiazole (4) (0.03 g, 24%), m.p. 203—204 °C; $\nu_{max.}$ (KBr) 1 325 and 1 155 $cm^{-1}$ ($SO_2$).

Evaporation of the second fraction gave the starting material (8) (0.088 g).

Evaporation of the third fraction gave a solid which was crystallised from ethanol to give crystals of *4-acetyl-2-methylsulphonyl-5-(1-oxido-4-pyridyl)-4,5-dihydro-1,3,4-thiadiazole* (10) (0.016 g, 10%), m.p. 163—164 °C (Found: C, 39.8; H, 3.5; N, 13.9. $C_{10}H_{11}N_3O_4S_2$ requires C, 39.9; H, 3.7; N, 13.9%); *m/z* 301 ($M^+$) and 285 ($M^+ - O$); $\nu_{max.}$ (KBr) 1 690 (C=O), 1 260 (N→O), 1 325 and 1 155 $cm^{-1}$ ($SO_2$); $\delta_H$ ($CDCl_3$) 2.36 (3 H, s, $COCH_3$), 3.30 (3 H, s, $SO_2CH_3$), 7.13 (1 H, s, 5-H), 7.31 (2 H, d, ArH), and 8.22 (2 H, d, ArH); $\delta_C$ ($CDCl_3$) 22.22 ($COCH_3$), 42.19 ($SO_2CH_3$), 71.07 (C-5), 124.21 (Ar C-3′, -5′), 135.89 (Ar C-4′), 139.75 (Ar C-2′, -6′), 151.84 (C-2), and 169.85 ($COCH_3$).

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