Oxidation of 3-Acetyl-5-methylthio-2-phenyl-2,3-dihydro-1,3,4-thiadiazole with *m*-Chloroperbenzoic Acid and Nucleophilic Substitution of the Oxidation Product, 3-Acetyl-5-methylsulphinyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole. *X*-Ray Molecular Structure of (2*S**)-3-Acetyl-5-[(*R**)-methylsulphinyl]-2-phenyl-2,3-dihydro-1,3,4-thiadiazole and of (1*R**,2*S**)-3-Acetyl-5-[(*S**)-methylsulphinyl]-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-Oxide

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3-Acetyl-5-methylthio-2-phenyl-2,3-dihydro-1,3,4-thiadiazole (**1**) was oxidized to 3-acetyl-5-methylsulphonyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxide (**9**) with *m*-chloroperbenzoic acid by way of diastereoisomeric mixtures of 3-acetyl-5-methylsulphinyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazoles (**7a**) and (**7b**) and 3-acetyl-5-methylsulphinyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxides (**8a**) and (**8b**). The relative stereochemistry of compounds (**7a**) and (**8b**) was established by *X*-ray crystallographic analysis. 5-Substituted 3-acetyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazoles were synthesized by substitution of the methylsulphinyl groups of compounds (**7a**) and (**7b**) with several nucleophiles.

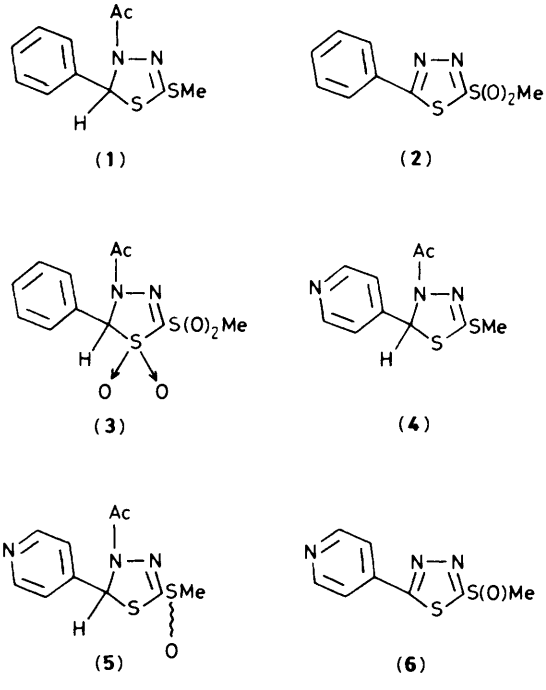
In our previous papers, we reported that the oxidation of 3-acetyl-5-methylthio-2-phenyl-2,3-dihydro-1,3,4-thiadiazole (**1**) with potassium permanganate gave 2-methylsulphonyl-5-phenyl-1,3,4-thiadiazole (**2**) and 3-acetyl-5-methylsulphonyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1,1-dioxide (**3**),[1] and that the oxidation of 3-acetyl-5-methylthio-2-(4-pyridyl)-2,3-dihydro-1,3,4-thiadiazole (**4**) with 30% hydrogen peroxide in acetic acid gave an inseparable diastereoisomeric mixture of 3-acetyl-5-methylsulphinyl-2-(4-pyridyl)-2,3-dihydro-1,3,4-thiadiazoles (**5**) along with 2-methylsulphinyl-5-(4-pyridyl)-1,3,4-thiadiazole (**6**).[2]

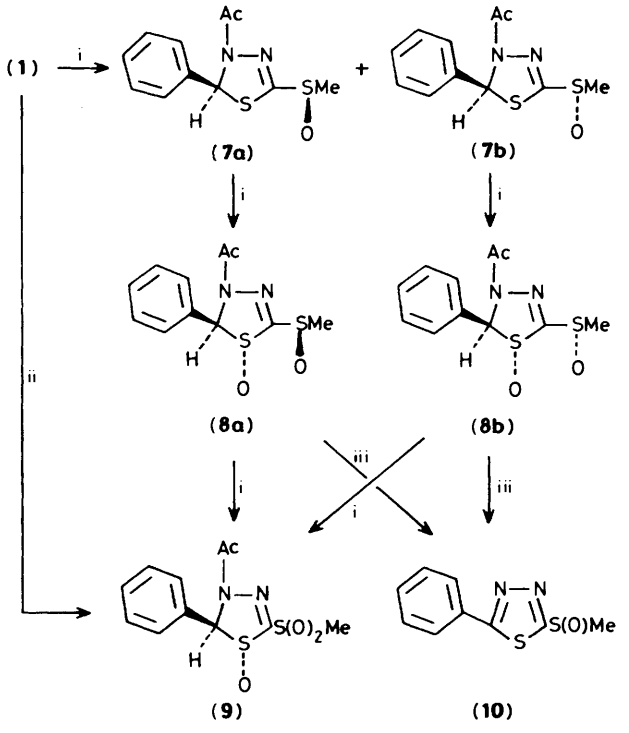
There are only a few reports on the synthesis of the diastereoisomers of 2,3-dihydro-1,3,4-thiadiazole derivatives. The cycloaddition reaction of sulphines (thione *S*-oxides) with diphenylnitrilimine ($PhC^{+}=N-\bar{N}Ph$) provided an inseparable diastereoisomeric mixture of the 2,3-dihydro-1,3,4-thiadiazole 1-oxides, or one strongly dominating isomer which is thermodynamically the more stable.[3,4]

Here we report the synthesis of diastereoisomers of 3-acetyl-5-methylsulphinyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazoles (**7a** and **b**) and of 3-acetyl-5-methylsulphinyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxides (**8a** and **b**), and the synthesis of 5-substituted 3-acetyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazoles by nucleophilic substitution of the methylsulphinyl group of compounds (**7a**) and (**7b**).

The oxidation of compound (**1**) with *m*-chloroperbenzoic acid (MCPBA) (3 mol equiv.) at room temperature gave 3-acetyl-5-methylsulphonyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxide (**9**), which was identical with the product obtained by oxidation of 3-acetyl-5-methylsulphonyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole with MCPBA.[1] The oxygen atom of the sulphoxide group of compound (**9**) was assigned as being *trans* to the phenyl group, since oxidation with MCPBA usually provides the isomer in which oxygen is bonded to the least hindered side of the sulphur.[5-7]

In the conversion of sulphides (**1**) into sulphone (**9**), several intermediates were observed by t.l.c. (Scheme). In order to clarify the reaction pathway, all intermediates were isolated by the use of different reaction conditions. Oxidation of compound (**1**) with MCPBA (1 mol equiv.) in chloroform at room temperature for 2 h gave compound (**7a**) (55%), m.p. 80—83 °C, and compound (**7b**) (35%), m.p. 127—129 °C. Both compounds (**7a**) and (**7b**) were shown to be diastereoisomers of 3-acetyl-5-methylsulphinyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazoles on the basis of their spectral data. The elemental analyses of both compounds agreed with the molecular formula $C_{11}H_{12}N_2O_2S_2$. The mass spectra of sulphoxides (**7a**) and (**7b**) showed the same





Scheme. *Reagents:* i, MCPBA (1 mol equiv.); ii, MCPBA (3 mol equiv.); iii, Et_3N–ethanol

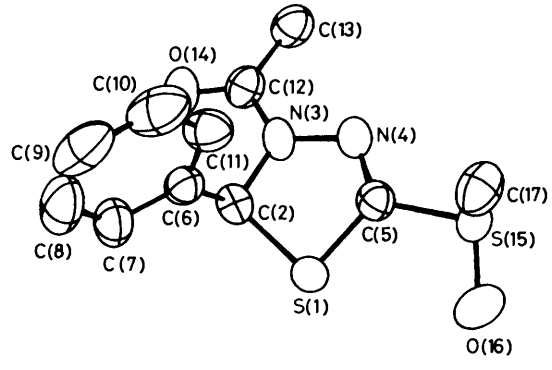


Figure 1. The molecular structure of compound (**7a**) (molecule A) showing the crystallographic numbering scheme

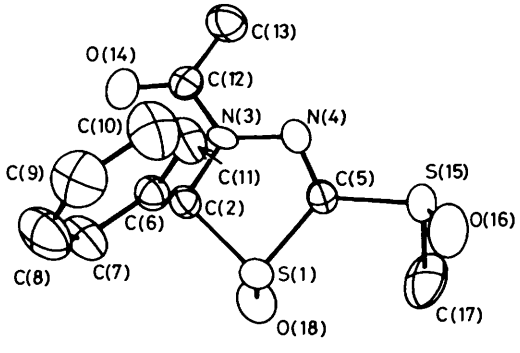


Figure 2. The molecular structure of compound (**8b**) showing the crystallographic numbering scheme

molecular-ion peak at *m/z* 268 and fragment-ion peaks at *m/z* 252 ($M^+ - O$) and *m/z* 163 [$(M^+ + 1) - COCH_3 - SOCH_3$]. Compounds (**7a**) and (**7b**) showed i.r. absorption, due to a 5-methylsulphinyl group, at 1 055 and 1 070 cm^{-1}, a ^1H n.m.r. signal for 5-methylsulphinyl protons at δ_H 2.90 and 2.95 (each singlet) and for 2-H protons at δ_H 7.08 and 7.07, and a ^{13}C n.m.r. signal due to sp^3-hybridized C-2 at δ_C 69.72 and 70.42, respectively. The detailed structure of compound (**7a**) which has an (*R**)-methylsulphinyl group was established by single-crystal *X*-ray analysis.

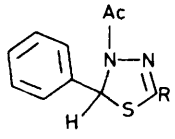
Oxidation of compound (**7a**) with MCPBA (1 mol equiv.) in chloroform at room temperature for 16 h gave 3-acetyl-5-methylsulphinyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxide (**8a**) (31%) as crystals, m.p. 155—158 °C. The structure of compound (**8a**) was assigned from the following spectral data. The chemical ionization mass spectrum (c.i.m.s.) showed a weak peak at *m/z* 302 $(M + NH_4)^+$ and a strong peak at *m/z* 225 [$(M^+ + 1) - CH_3CO_2H$]. The i.r. spectrum showed two strong absorptions at 1 070 and 1 060 cm^{-1} due to SO groups. The ^{13}C and ^1H n.m.r. spectra indicated the presence of an sp^3-hybridized C-2 (δ_C 85.90) and a 2-methine proton (δ_H 6.77), respectively.

Oxidation of compound (**7b**) with MCPBA (1 mol equiv.) in chloroform at room temperature for 24 h gave a single product, 3-acetyl-5-methylsulphinyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxide (**8b**) (76%), as crystals, m.p. 133—135 °C. The structure of compound (**8b**) was determined by the following spectral data and *X*-ray structure analysis. The c.i.m.s. showed a weak peak at *m/z* 302 $(M + NH_4)^+$ and a strong peak at *m/z* 225 as for compound (**8a**). The i.r. spectrum showed SO absorption at 1 070 and 1 055 cm^{-1}. The ^1H n.m.r. spectrum showed a signal for 5-methylsulphinyl protons at δ_H 3.17 and a signal for 2-H at δ_H 6.64. The ^{13}C n.m.r. spectrum indicated an sp^3-hybridized C-2 at δ_C 85.99. From these spectral data, compounds (**8a**) and (**8b**) were shown to be diastereoisomeric. The detailed structure of compound (**8b**), which has an (*S**)-methylsulphinyl group, was established by single-crystal *X*-ray analysis. The molecular structures of compounds (**7a**) and (**8b**) are illustrated in Figures 1 and 2.

Oxidation of compounds (**8a**) and (**8b**) with MCPBA (1.1 mol equiv.) in chloroform at room temperature for 24 h gave the same product, *viz.* 3-acetyl-5-methylsulphonyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxide (**9**).[1] Previously, we have reported that treatment of 3-acetyl-5-methylsulphonyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxide (**9**) with triethylamine in ethanol gave 2-methylsulphonyl-5-phenyl-1,3,4-thiadiazole (**10**).[1] Similarly, both compounds (**8a**) and (**8b**) with triethylamine gave compound (**10**) in almost quantitative yield. Formation of compounds (**9**) and (**10**) from both compounds (**8a**) and (**8b**) also supports the facts that compound (**8a**) is the diastereoisomer of compound (**8b**) and that the *S*-oxide (**9**) has the *trans* configuration discussed above.

From these results, it was concluded that compound (**1**) was oxidized to compound (**9**) by way of the diastereoisomeric intermediates (**7a**),(**7b**) and (**8a**),(**8b**), successively.

The nucleophilic substitution reaction at C-5 of compounds (**7a**) and (**7b**) was examined in relation to potential synthesis of 5-substituted 3-acetyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazoles, since the sulphinyl group is known to be a good leaving group.[8]



(**11**) R = H
(**12**) R = OEt
(**13**) R = $CH(CO_2Et)_2$
(**14**) R = SPh

Table 1. Fractional atomic co-ordinates for compound (**7a**) with e.s.d.s in parentheses

(a) Molecule A

Atom	*x*	*y*	*z*
S(1)	0.534 8(1)	0.148 9(1)	0.585 4(0)
C(2)	0.476 2(3)	0.260 1(2)	0.562 6(1)
N(3)	0.478 3(2)	0.239 0(2)	0.521 5(1)
N(4)	0.548 1(2)	0.161 6(2)	0.511 6(1)
C(5)	0.584 6(3)	0.114 4(2)	0.541 3(1)
C(6)	0.558 0(3)	0.343 4(2)	0.575 2(1)
C(7)	0.520 9(4)	0.401 5(2)	0.603 7(1)
C(8)	0.597 3(5)	0.480 0(2)	0.615 2(1)
C(9)	0.707 9(5)	0.498 1(3)	0.598 7(1)
C(10)	0.746 3(4)	0.439 8(3)	0.570 5(1)
C(11)	0.671 3(4)	0.363 0(2)	0.559 2(1)
C(12)	0.405 6(3)	0.291 5(2)	0.494 7(1)
C(13)	0.413 3(4)	0.265 5(2)	0.453 7(1)
O(14)	0.341 8(2)	0.355 3(2)	0.505 3(1)
S(15)	0.672 8(1)	0.006 8(1)	0.538 5(0)
O(16)	0.656 9(3)	−0.041 7(2)	0.575 3(1)
C(17)	0.827 6(3)	0.060 0(2)	0.543 6(1)

(b) Molecule B

Atoms	*x*	*y*	*z*
S(1)	0.171 6(1)	0.531 5(1)	0.186 5(0)
C(2)	0.190 9(3)	0.644 0(2)	0.162 0(1)
N(3)	0.307 0(2)	0.682 6(2)	0.182 6(1)
N(4)	0.341 2(3)	0.647 4(2)	0.218 9(1)
C(5)	0.276 2(3)	0.573 3(2)	0.223 7(1)
C(6)	0.075 0(3)	0.704 9(2)	0.163 3(1)
C(7)	−0.024 9(3)	0.694 2(2)	0.134 8(1)
C(8)	−0.134 0(4)	0.747 3(3)	0.135 4(1)
C(9)	−0.145 5(4)	0.811 4(3)	0.164 0(1)
C(10)	−0.046 9(4)	0.821 7(3)	0.192 3(1)
C(11)	0.063 6(3)	0.769 0(2)	0.192 3(1)
C(12)	0.370 0(3)	0.757 7(2)	0.168 6(1)
C(13)	0.482 6(4)	0.795 1(3)	0.192 9(1)
O(14)	0.332 3(3)	0.787 8(2)	0.137 1(1)
S(15)	0.297 8(1)	0.507 3(1)	0.267 3(0)
O(16)	0.240 6(4)	0.414 0(2)	0.257 5(1)
C(17)	0.177 2(6)	0.568 6(4)	0.290 9(1)

Reaction of a diastereoisomeric mixture (**7a**) and (**7b**) with sodium borohydride at room temperature for 2 h led to the smooth reductive elimination of the methylsulphinyl group to give 3-acetyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole (**11**) (78%). The reaction of the mixture of compounds (**7a**) and (**7b**) with sodium ethoxide in ethanol at 0 °C for 0.5 h gave 3-acetyl-5-ethoxy-2-phenyl-2,3-dihydro-1,3,4-thiadiazole (**12**) (70%). Reaction of the mixture of sulphoxides (**7a**) and (**7b**) with diethyl malonate in the presence of sodium hydride at room temperature for 2 h afforded diethyl (4-acetyl-5-phenyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)malonate (**13**) (59%). Reaction of the mixture of compounds (**7a**) and (**7b**) with thiophenol in the presence of sodium hydride at 0 °C for 10 min afforded 3-acetyl-2-phenyl-5-phenylthio-2,3-dihydro-1,3,4-thiadiazole (**14**) (86%).

X-Ray Crystal Structures of Compounds (**7a**) *and* (**8b**).—The atomic co-ordinates, bond lengths, bond angles, and torsion angles of the non-hydrogen atoms of compounds (**7a**) and (**8b**) are listed in Tables 1—5. Compound (**7a**) contains two molecules in the asymmetric unit. The two independent molecules (A and B) have similar geometries (Tables 1, 2, and 5) and the conformation of molecule A is shown in Figure 1.

The configurations of compounds (**7a**) and (**8b**) are different at the methylsulphinyl moiety, S(15)–O(16). Compound (**7a**) has an (*R**)-methylsulphinyl group while compound (**8b**) has an

Table 2. Bond lengths (Å) and angles (°) for compound (**7a**) with e.s.d.s in parentheses

(a) Bond lengths (Å)

	Molecule A	Molecule B
S(1)–C(2)	1.846(3)	1.831(3)
S(1)–C(5)	1.746(4)	1.728(3)
C(2)–N(3)	1.473(5)	1.462(4)
C(2)–C(6)	1.501(4)	1.493(4)
N(3)–N(4)	1.380(4)	1.382(5)
N(3)–C(12)	1.372(4)	1.367(4)
N(4)–C(5)	1.266(5)	1.271(4)
C(5)–S(15)	1.790(3)	1.788(3)
C(6)–C(7)	1.378(5)	1.386(5)
C(6)–C(11)	1.386(5)	1.376(5)
C(7)–C(8)	1.407(5)	1.370(5)
C(8)–C(9)	1.366(7)	1.366(6)
C(9)–C(10)	1.376(6)	1.372(5)
C(10)–C(11)	1.379(5)	1.377(5)
C(12)–C(13)	1.492(5)	1.487(5)
C(12)–O(14)	1.203(4)	1.215(5)
S(15)–O(16)	1.484(3)	1.479(3)
S(15)–C(17)	1.782(3)	1.796(6)

(b) Bond angles (°)

	Molecule A	Molecule B
C(2)–S(1)–C(5)	88.3(1)	88.0(2)
S(1)–C(2)–N(3)	102.4(2)	102.5(2)
S(1)–C(2)–C(6)	112.7(2)	111.3(2)
N(3)–C(2)–C(6)	112.8(3)	114.2(3)
C(2)–N(3)–N(4)	117.6(3)	116.9(3)
C(2)–N(3)–C(12)	120.1(3)	121.4(3)
N(4)–N(3)–C(12)	122.2(3)	121.2(3)
N(3)–N(4)–C(5)	109.9(3)	108.9(3)
S(1)–C(5)–N(4)	119.2(2)	119.6(3)
S(1)–C(5)–S(15)	119.0(2)	119.1(2)
N(4)–C(5)–S(15)	121.5(3)	121.2(3)
C(2)–C(6)–C(7)	119.5(3)	118.4(3)
C(2)–C(6)–C(11)	121.7(3)	122.0(3)
C(7)–C(6)–C(11)	118.9(3)	119.5(3)
C(6)–C(7)–C(8)	119.3(4)	120.3(3)
C(7)–C(8)–C(9)	120.6(3)	120.4(3)
C(8)–C(9)–C(10)	120.4(4)	119.3(4)
C(9)–C(10)–C(11)	118.9(4)	121.2(4)
C(10)–C(11)–C(6)	121.9(3)	119.2(3)
N(3)–C(12)–C(13)	116.7(3)	117.1(3)
N(3)–C(12)–O(14)	119.0(3)	118.2(3)
C(13)–C(12)–O(14)	124.3(3)	124.7(3)
C(5)–S(15)–O(16)	104.3(2)	104.6(2)
C(5)–S(15)–C(17)	95.9(2)	95.8(2)
O(16)–S(15)–C(17)	106.4(2)	104.6(3)

(*S**)-methylsulphinyl group as shown in Figure 3. Their geometries are very similar to each other except at the sulphinyl group. The thiadiazoline† rings adopt a half-chair form, in which puckering is apparent at the C(2) atoms with displacements of −0.101 and 0.126 Å respectively for molecules A and B of compound (**7a**), and of −0.146 Å for compound (**8b**). In compound (**8b**), the oxygen atom attached to S(1) lies on the opposite side of the thiadiazoline ring in relation to the phenyl group.

The acetylhydrazino moieties C(13)–O(14)–C(12)–N(3)–N(4)–C(2) are nearly planar in compounds (**7a**) and (**8b**). Their displacements from their mean planes vary from −0.025 to 0.027 Å [molecule A of (**7a**)], −0.021 to 0.044 Å [molecule B of (**7a**)], and −0.032 to 0.029 Å [compound (**8b**)].

† 2,3-Dihydrothiadiazole.

Table 3. Fractional atomic co-ordinates for compound (**8b**) with e.s.d.s in parentheses

Atom	*x*	*y*	*z*
S(1)	0.548 0(0)	0.801 8(0)	0.565 6(1)
C(2)	0.625 9(1)	0.821 2(1)	0.723 8(4)
N(3)	0.588 4(1)	0.864 7(1)	0.852 9(3)
N(4)	0.522 5(1)	0.897 8(1)	0.801 5(3)
C(5)	0.498 9(2)	0.877 3(1)	0.655 3(4)
C(6)	0.692 8(2)	0.856 1(1)	0.632 9(4)
C(7)	0.753 3(2)	0.816 3(2)	0.569 0(5)
C(8)	0.815 3(2)	0.847 1(2)	0.483 2(6)
C(9)	0.816 6(2)	0.917 5(2)	0.458 3(5)
C(10)	0.756 8(2)	0.956 5(2)	0.522 6(6)
C(11)	0.695 0(2)	0.926 8(2)	0.609 6(5)
C(12)	0.617 3(2)	0.872 1(1)	1.018 5(4)
C(13)	0.576 6(2)	0.920 6(2)	1.137 5(4)
O(14)	0.674 6(1)	0.839 2(1)	1.058 2(3)
S(15)	0.415 8(0)	0.919 5(0)	0.561 3(1)
O(16)	0.439 9(1)	0.948 3(1)	0.393 8(3)
C(17)	0.362 4(2)	0.843 1(2)	0.512 2(7)
O(18)	0.501 4(1)	0.742 3(1)	0.628 4(4)

Table 4. Bond lengths (Å) and angles (°) for compound (**8b**) with e.s.d.s in parentheses

(a) Bond lengths (Å)

S(1)–C(2)	1.848(3)	C(6)–C(11)	1.383(4)
S(1)–C(5)	1.824(3)	C(7)–C(8)	1.387(5)
S(1)–O(18)	1.484(2)	C(8)–C(9)	1.377(5)
C(2)–N(3)	1.455(3)	C(9)–C(10)	1.368(5)
C(2)–C(6)	1.506(4)	C(10)–C(11)	1.380(5)
N(3)–N(4)	1.359(3)	C(12)–C(13)	1.488(4)
N(3)–C(12)	1.379(4)	C(12)–O(14)	1.209(3)
N(4)–C(5)	1.263(4)	S(15)–O(16)	1.468(3)
C(5)–S(15)	1.795(3)	S(15)–C(17)	1.781(4)
C(6)–C(7)	1.382(4)		

(b) Bond angles ( )

C(2)–S(1)–C(5)	85.4(1)	C(2)–C(6)–C(11)	121.8(2)
C(2)–S(1)–O(18)	109.3(1)	C(7)–C(6)–C(11)	119.0(3)
C(5)–S(1)–O(18)	104.5(1)	C(6)–C(7)–C(8)	120.4(3)
S(1)–C(2)–N(3)	104.6(2)	C(7)–C(8)–C(9)	120.3(3)
S(1)–C(2)–C(6)	109.5(2)	C(8)–C(9)–C(10)	119.0(3)
N(3)–C(2)–C(6)	113.3(2)	C(9)–C(10)–C(11)	121.4(3)
C(2)–N(3)–N(4)	116.1(2)	C(10)–C(11)–C(6)	119.8(3)
C(2)–N(3)–C(12)	122.5(2)	N(3)–C(12)–C(13)	118.0(2)
N(4)–N(3)–C(12)	121.4(2)	N(3)–C(12)–O(14)	118.1(3)
N(3)–N(4)–C(5)	112.3(2)	C(13)–C(12)–O(14)	123.9(3)
S(1)–C(5)–N(4)	116.3(2)	C(5)–S(15)–O(16)	107.8(1)
S(1)–C(5)–S(15)	125.3(2)	C(5)–S(15)–C(17)	96.6(2)
N(4)–C(5)–S(15)	118.2(2)	O(16)–S(15)–C(17)	105.9(2)
C(2)–C(6)–C(7)	119.2(2)		

As shown in Tables 2 and 4, the lengths of the N(3)–C(12) bond are similar to that of a peptide bond and the bond angles around the N(3) atoms are close to 120° for sp^2 hybridization. The C(5) atoms deviate from the planes of the acetylhydrazino moieties by 0.266, 0.165, and 0.212 Å for molecules A and B of compound (**7a**) and for compound (**8b**), respectively. The endocyclic bond angles around the N(4) atoms are close to the normal tetrahedral value.

Experimental

M.p.s were determined by the capillary method and are uncorrected. I.r. spectra were recorded on a Hitachi 215 spectrometer. ^{1}H N.m.r. spectra were recorded on a JEOL-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 Merck Kieselgel (70—230 mesh) and Mallinckrodt silicic acid (100 mesh) was employed. Oxidation reactions were carried out under argon.

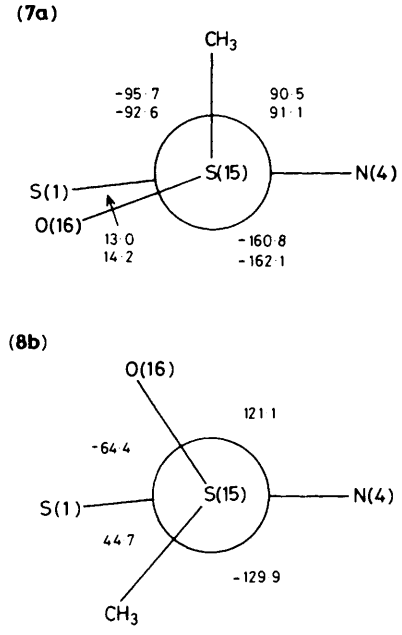


Figure 3. Configurations of the methylsulphinyl group of compounds (**7a**) and (**8b**) showing the torsion angles

Table 5. Torsion angles (°) in molecules A and B of compound (**7a**) and in compound (**8b**)

	(**7a**)-A	(**7a**)-B	(**8b**)
C(5)–S(1)–C(2)–N(3)	13.6	16.8	19.7
C(5)–S(1)–C(2)–C(6)	−107.9	−105.7	−102.0
C(2)–S(1)–C(5)–N(4)	−11.5	−12.7	−17.9
C(2)–S(1)–C(5)–S(15)	174.6	171.0	167.5
S(1)–C(2)–N(3)–N(4)	−16.0	−20.9	−21.4
S(1)–C(2)–N(3)–C(12)	159.7	166.8	158.3
C(6)–C(2)–N(3)–N(4)	105.5	99.7	97.7
C(6)–C(2)–N(3)–C(12)	−78.9	−72.7	−82.5
S(1)–C(2)–C(6)–C(7)	−98.0	−87.3	−92.1
S(1)–C(2)–C(6)–C(11)	81.2	91.1	87.1
N(3)–C(2)–C(6)–C(7)	146.6	157.2	151.6
N(3)–C(2)–C(6)–C(11)	−34.2	−24.5	−29.2
C(2)–N(3)–N(4)–C(5)	9.0	13.2	9.2
C(12)–N(3)–N(4)–C(5)	−166.5	−174.4	−170.5
C(2)–N(3)–C(12)–C(13)	180.0	176.4	177.0
C(2)–N(3)–C(12)–O(14)	0.9	−5.1	−2.4
N(4)–N(3)–C(12)–C(13)	−4.6	4.4	−3.3
N(4)–N(3)–C(12)–O(14)	176.3	−177.1	177.3
N(3)–N(4)–C(5)–S(1)	3.9	2.5	8.8
N(3)–N(4)–C(5)–S(15)	177.7	178.7	−176.1
S(1)–C(5)–S(15)–O(16)	13.0	14.2	−64.3
S(1)–C(5)–S(15)–C(17)	−95.7	−92.6	44.7
N(4)–C(5)–S(15)–O(16)	−160.8	−162.1	121.1
N(4)–C(5)–S(15)–C(17)	90.5	91.1	−129.9
C(2)–C(6)–C(7)–C(8)	−179.5	178.6	179.4
C(2)–C(6)–C(11)–C(10)	179.6	−178.6	−178.8
O(18)–S(1)–C(2)–N(3)			−84.0
O(18)–S(1)–C(2)–C(6)			154.2
O(18)–S(1)–C(5)–N(4)			90.9
O(18)–S(1)–C(5)–S(15)			−83.8

Oxidation of 3-Acetyl-5-methylthio-2-phenyl-2,3-dihydro-1,3,4-thiadiazole (**1**) *with MCPBA.—Method A.* A solution of 85% MCPBA (1.21 g, 5.96 mmol) in $CHCl_3$ (20 ml) was added dropwise to a stirred solution of 3-acetyl-5-methylthio-2-phenyl-2,3-dihydro-1,3,4-thiadiazole (**1**) (500 mg, 1.98 mmol) in $CHCl_3$ (4 ml) at room temperature. After being stirred at room temperature for 1 h, the mixture was neutralized with 5% aqueous sodium hydrogen carbonate and was then extracted with $CHCl_3$ (3 × 100 ml). The combined extracts were washed with brine, and dried (anhydrous Na_2SO_4). After removal of the solvent by evaporation, the residue was crystallized from ethanol to give crystals of (1*R**,2*S**)-3-acetyl-5-methylsulphonyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxide (**9**) (553 mg, 93%), m.p. 136—138 °C (lit.,[1] 136—138 °C)

Method B. A solution of 80% MCPBA (428 mg, 1.98 mmol) in $CHCl_3$ (16 ml) was added dropwise to an ice-cooled stirred solution of 3-acetyl-5-methylthio-2-phenyl-2,3-dihydro-1,3,4-thiadiazole (**1**) (500 mg, 1.98 mmol) in $CHCl_3$ (5 ml). After being stirred at room temperature for 2 h, the mixture was neutralized with 5% aqueous sodium hydrogen carbonate and was then extracted with $CHCl_3$ (3 × 100 ml). The combined extracts were washed with brine and dried (anhydrous Na_2SO_4). After removal of the solvent by evaporation, the residue was chromatographed on silica gel with $CHCl_3$–acetone (50:1) as eluant to give the starting material (**1**) (36 mg), and (2*S**)-3-*acetyl*-5-[(R*)-*methylsulphinyl*]-2-*phenyl*-2,3-*dihydro*-1,3,4-*thiadiazole* (**7a**) (292 mg, 55%), m.p. 80—83 °C (from ethanol) (Found: C, 49.4; H, 4.5; N, 10.7. $C_{11}H_{12}N_2O_2S_2$ requires C, 49.2; H, 4.5; N, 10.4%); $\nu_{max.}$(KBr) 1 675 (C=O) and 1 055 cm^{-1} (SOMe); $\delta_H(CDCl_3)$ 2.30 (3 H, s, COMe), 2.90 (3 H, s, SOMe), 7.08 (1 H, s, 2-H), and 7.16—7.44 (5 H, m, Ph); $\delta_C[(CD_3)_2SO]$ 21.98 (COMe), 41.17 (SOMe), 69.72 (C-2), 125.44—140.56 (Ar), 159.45 (C-5), and 168.83 (C=O); *m/z* 268 (M^+) 252 ($M^+ - O$), and 163 [$(M^+ + 1) - COCH_3 - SOCH_3$], and (2*S**)-3-*acetyl*-5-[(S*)-*methylsulphinyl*]-2-*phenyl*-2,3-*dihydro*-1,3,4-*thiadiazole* (**7b**) (185 mg, 35%), m.p. 127—129 °C (from ethanol) (Found: C, 49.2; H, 4.4; N, 10.1%); $\nu_{max.}$(KBr) 1 665 (C=O) and 1 070 cm^{-1} (SOMe); $\delta_H(CDCl_3)$ 2.31 (3 H, s, COMe), 2.95 (3 H, s, SOMe), 7.07 (1 H, s, 2-H), and 7.31 (5 H, s, Ph); $\delta_C[(CD_3)_2SO]$ 22.04 (COMe), 40.29 (SOMe), 70.42 (C-2), 125.46—140.39 (Ar), 159.54 (C-5), and 168.83 (C=O); *m/z* 268 (M^+), 252 ($M^+ - O$), and 163 [$(M^+ + 1) - COCH_3 - SOCH_3$].

(1R*,2S*)-3-*Acetyl*-5-[(R*)-*methylsulphinyl*-2-*phenyl*-2,3-*dihydro*-1,3,4-*thiadiazole* 1-*Oxide* (**8a**).—A solution of 85% MCPBA (69 mg, 0.34 mmol) in $CHCl_3$ (8 ml) was added dropwise to an ice-cooled stirred solution of the 2,3-dihydro-1,3,4-thiadiazole (**7a**) (90 mg, 0.34 mmol) in $CHCl_3$ (4 ml). After being stirred at room temperature for 16 h, the mixture was neutralized with 5% aqueous sodium hydrogen carbonate and was then extracted with $CHCl_3$ (3 × 70 ml). The combined extracts were washed with brine, and dried (anhydrous Na_2SO_4). After removal of the solvent by evaporation, the residue was chromatographed on silica gel with $CHCl_3$-acetone (50:1) as eluant to give the starting material (**7a**) (28 mg) and a solid which was crystallized from ethanol to give *compound* (**8a**) (30 mg, 31%), m.p. 155—158 °C (Found: C, 46.5; H, 4.15; N, 9.55. $C_{11}H_{12}N_2O_3S_2$ requires C, 46.5; H, 4.25; N, 9.85%); $\nu_{max.}$(KBr) 1 710 (C=O), 1 070, and 1 060 cm^{-1} (SOMe); $\delta_H(CDCl_3)$ 2.57 (3 H, s, COMe), 2.98 (3 H, s, SOMe), 6.77 (1 H, s, 2-H), 7.03—7.21 (2 H, m, ArH), and 7.33—7.51 (3 H, m, ArH); $\delta_C[(CD_3)_2SO]$ 21.75 (COMe), 40.99 (SOMe), 85.90 (C-2), 126.14—129.49 (Ar), 160.42 (C-5), and 169.03 (C=O); *m/z* (NH_3; c.i.m.s.) 302 (M^+ + 1) and 225 [$(M^+ + 1) - CH_3CO_2H$].

(1R*,2S*)-3-*Acetyl*-5-[(S*)-*methylsulphinyl*]-2-*phenyl*-2,3-*dihydro*-1,3,4-*thiadiazole* 1-*Oxide* (**8b**).—A solution of 80% MCPBA (205 mg, 0.95 mmol) in $CHCl_3$ (15 ml) was added dropwise to an ice-cooled stirred solution of the 2,3-dihydro-1,3,4-thiadiazole (**7b**) (250 mg, 0.93 mmol) in $CHCl_3$ (5 ml). After being stirred at room temperature for 24 h, the mixture was neutralized with 5% aqueous sodium hydrogen carbonate and was then extracted with $CHCl_3$ (3 × 100 ml). The combined extracts were washed with brine and dried (anhydrous Na_2SO_4). After removal of the solvent by evaporation, the residue was chromatographed on silica gel with $CHCl_3$–acetone (50:1) as eluant to give a solid which was crystallized from ethanol to give *compound* (**8b**) (202 mg, 76%), m.p. 133—135 °C (Found: C, 46.2; H, 4.1; N, 9.55%); $\nu_{max.}$(KBr) 1 695 (C=O), 1 070, and 1 055 cm^{-1} (SOMe); $\delta_H(CDCl_3)$ 2.54 (3 H, s, COMe), 3.17 (3 H, s, SOMe), 6.64 (1 H, s, 2-H), 6.99—7.20 (2 H, m, ArH), and 7.25—7.48 (3 H, m, ArH); $\delta_C[(CD_3)_2SO]$ 21.84 (COMe), 41.96 (SOMe), 85.99 (C-2), 126.31—129.52 (Ar), 159.31 (C-5), and 169.03 (C=O); *m/z* (NH_3; c.i.m.s.) 302 (M + NH_4)$^+$ and 225 [$(M^+ + 1) - CH_3CO_2H$].

Oxidation of Compounds (**8a**) *and* (**8b**) *with MCPBA.—Method A.* A solution of 80% MCPBA (125 mg, 0.58 mmol) in $CHCl_3$ (8 ml) was added dropwise to a stirred solution of the 2,3-dihydro-1,3,4-thiadiazole 1-oxide (**8a**) (150 mg, 0.53 mmol) in $CHCl_3$ (5 ml) at room temperature. After being stirred at room temperature for 24 h, the mixture was neutralized with 5% aqueous sodium hydrogen carbonate and was then extracted with $CHCl_3$ (3 × 70 ml). The combined extracts were washed with brine, and dried (anhydrous Na_2SO_4). After removal of the solvent by evaporation, the residue was crystallized from ethanol to give compound (**9**) (156 mg, 98%).

Method B. A solution of 80% MCPBA (84 mg, 0.39 mmol) in $CHCl_3$ (7 ml) was added dropwise to a stirred solution of the 2,3-dihydro-1,3,4-thiadiazole 1-oxide (**8b**) (100 mg, 0.35 mmol) in $CHCl_3$ (5 ml) at room temperature. Work-up as in method A gave crystals of compound (**9**) (105 mg, 99%).

Conversion of Compounds (**8a**) *and* (**8b**) *into 2-Methylsulphinyl-5-phenyl-1,3,4-thiadiazole* (**10**).—*Method A.* A solution of triethylamine (64 mg, 0.63 mmol) in ethanol (2 ml) was added dropwise to a stirred suspension of compound (**8a**) (90 mg, 0.32 mmol) in ethanol (6 ml) at room temperature. After the mixture had been stirred at room temperature for 15 min, the solvent was evaporated off under reduced pressure. The residue was crystallized from ethanol–ether to give *2-methylsulphinyl-5-phenyl-1,3,4-thiadiazole* (**10**) (65 mg, 91%), m.p. 110—111 °C (Found: C, 48.4; H, 3.4; N, 12.6. $C_9H_8N_2OS_2$ requires C, 48.2; H, 3.6; N, 12.5%); $\nu_{max.}$(KBr) 1 050 cm^{-1} (SO); $\delta_H(CDCl_3)$ 3.14 (3 H, s, SOMe), 7.42—7.60 (3 H, m, ArH), and 7.90—8.04 (2 H, m, ArH); *m/z* 224 (M^+).

Method B. A solution of triethylamine (130 mg, 1.28 mmol) in ethanol (2 ml) was added dropwise to a stirred suspension of compound (**8b**) (180 mg, 0.63 mmol) in ethanol (10 ml). Work-up as in method A gave crystals of compound (**10**) (136 mg, 96%).

3-Acetyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole (**11**).—A solution of the diastereoisomeric mixture of the 2,3-dihydro-1,3,4-thiadiazoles (**7a** and **b**)† (500 mg, 1.87 mmol) in tetrahydrofuran (THF) (4 ml) was added dropwise to an ice-cooled stirred solution of $NaBH_4$ (78 mg, 2.06 mmol) in THF (2 ml). After 1 h at room temperature, water (2 ml) was added to the reaction mixture, which was then extracted with $CHCl_3$ (3 × 100 ml). The combined extracts were washed with brine, and dried (anhydrous Na_2SO_4). After removal of the solvent by evaporation, the residue was chromatographed on silica gel with $CHCl_3$–acetone (50:1) as eluant to give a solid which was

† The mixture was prepared by oxidation of the 2,3-dihydro-1,3,4-thiadiazole (**1**) with MCPBA and was purified by chromatography. The diastereoisomeric ratio of (**7a**) to (**7b**) was *ca.* 3:2.

crystallized from light petroleum (b.p. 30—70 °C)–ethanol to give *compound* (**11**) (300 mg, 78%), m.p. 86—88 °C (Found: C, 58.2; H, 4.8; N, 13.65. $C_{10}H_{10}N_2OS$ requires C, 58.2; H, 4.9; N, 13.6%); $\nu_{max.}$(KBr) 1 655 cm^{-1} (C=O); $\delta_H(CDCl_3)$ 2.32 (3 H, s, COMe), 6.90 (1 H, s, 2-H), 7.29 (5 H, s, Ph), and 7.36 (1 H, s, 5-H); *m/z* 206 (M^+) and 163 ($M^+ - COCH_3$).

3-*Acetyl*-5-*ethoxy*-2-*phenyl*-2,3-*dihydro*-1,3,4-*thiadiazole* (**12**).—A solution of the diastereoisomeric mixture of compounds (**7a** and **b**) (200 mg, 0.75 mmol) in ethanol (3 ml) was added dropwise to an ice-cooled stirred solution of sodium ethoxide (102 mg, 1.5 mmol) in ethanol (3 ml). After 30 min at 0 °C, the mixture was treated with water (2 ml) and was then neutralized with acetic acid and extracted with $CHCl_3$ (3 × 100 ml). The combined extracts were washed with brine, and dried (anhydrous Na_2SO_4). After removal of the solvent by evaporation, the residue was chromatographed on silica gel with $CHCl_3$–acetone (50:1) as eluant to give a solid which was crystallized from light petroleum to afford *compound* (**12**) (130 mg, 70%), m.p. 86—88 °C (Found: C, 57.6; H, 5.6; N, 10.9. $C_{12}H_{14}N_2O_2S$ requires C, 57.6; H, 5.6; N, 11.2%); $\nu_{max.}$(KBr) 1 650 cm^{-1} (C=O); $\delta_H(CDCl_3)$ 1.39 (3 H, t, CH_2Me), 2.24 (3 H, s, COMe), 4.36 (2 H, q, CH_2Me), 7.07 (1 H, s, 2-H), and 7.32 (5 H, s, Ph); *m/z* 250 (M^+), 208 [($M^+ + 1$) − $COCH_3$], and 162 ($M^+ - COCH_3 - OC_2H_5$).

Diethyl (4-*Acetyl*-5-*phenyl*-4,5-*dihydro*-1,3,4-*thiadiazol*-2-*yl*)-*malonate* (**13**).—A suspension of sodium hydride (90 mg, 60% dispersion in oil; washed 2 × with ether) in anhydrous THF (2 ml) was added dropwise to a stirred solution of diethyl malonate (359 mg, 2.24 mmol) in anhydrous THF (2 ml) at 0 °C. After 1 h at room temperature, the mixture was treated dropwise with a solution of the diastereoisomeric mixture of compounds (**7a** and **b**) (300 mg, 1.12 mmol) in anhydrous THF (3 ml). After being stirred for 2 h, the mixture was neutralized with aqueous acetic acid, and was extracted with $CHCl_3$ (3 × 100 ml). The combined extracts were washed with brine, dried (anhydrous Na_2SO_4), and evaporated under reduced pressure. The residue was chromatographed on silica gel with $CHCl_3$–acetone (50:1) as eluant to give *compound* (**13**) as an oil (241 mg, 59%) (Found: M^+, 364.1105. $C_{17}H_{20}N_2O_5S$ requires *M*, 364.1093); $\nu_{max.}$(film) 1 730 ($CO_2C_2H_5$), and 1 675 cm^{-1} (COMe); $\delta_H(CDCl_3)$ 1.24 (3 H, t, CH_2Me), 1.30 (3 H, t, CH_2Me), 2.28 (3 H, s, COMe), 4.22 (2 H, q, CH_2Me), 4.26 (2 H, q, CH_2Me), 4.70 (1 H, s, CH), 6.98 (1 H, s, 2-H), and 7.20—7.48 (5 H, m, Ph); *m/z* 364 (M^+) and 322 [($M^+ + 1$) − $COCH_3$].

3-*Acetyl*-2-*phenyl*-5-*phenylthio*-2,3-*dihydro*-1,3,4-*thiadiazole* (**14**).—A suspension of sodium hydride (60 mg, 60% dispersion in oil; washed 2 × with ether) in anhydrous THF (5 ml) was added dropwise to a stirred solution of thiophenol (165 mg, 1.5 mmol) in anhydrous THF (5 ml) at 0 °C. After 1 h at room temperature, the mixture was cooled to 0 °C and treated dropwise with a solution of the diastereoisomeric mixture of compounds (**7a** and **b**) (200 mg, 0.75 mmol) in anhydrous THF (5 ml). After being stirred for 10 min, the mixture was neutralized with aqueous acetic acid and was extracted with $CHCl_3$ (3 × 100 ml). The combined extracts were washed with brine, dried (anhydrous Na_2SO_4), and evaporated under reduced pressure. The residue was chromatographed on silica gel with $CHCl_3$–acetone (50:1) as eluant to give a solid which was crystallized from ethanol to afford *compound* (**14**) (201 mg, 86%), m.p. 101—102 °C (Found: C, 61.2; H, 4.4; N, 8.9. $C_{16}H_{14}N_2OS_2$ requires C, 61.1; H, 4.5; N, 8.9%); $\nu_{max.}$(KBr) 1 670 cm^{-1} (C=O); $\delta_H(CDCl_3)$ 2.27 (3 H, s, COMe), 6.93 (1 H, s, 2-H), 7.26 (5 H, s, 2-Ph), and 7.30—7.70 (5 H, m, SPh); *m/z* 314 (M^+) and 272 [($M^+ + 1$) − $COCH_3$].

Structure Determinations of Compounds (**7a**) *and* (**8b**) *by X-Ray Diffraction.*—Crystals of both compounds (**7a**) and (**8b**) were grown from ethyl acetate solution. The crystals of compound (**7a**), dimensions 0.5 × 0.5 × 0.3 mm, and of (**8b**) 0.25 × 0.6 mm, were mounted on a Rigaku four-circle diffractometer. The intensity data for reflections with $2 < 2\theta < 50°$ were collected using graphite-monochromated Mo-K_α radiation (λ 0.7107 Å), with ω (**7a**) and 2θ/ω (**8b**) scan modes. The data were corrected for Lorentz and polarization factors and background effects, but not for absorption. The independent reflections, 3 383 ($F > 6\sigma F$) for (**7a**) and 2 075 ($F > \sigma F$) for (**8b**), were used in all calculations.

Crystal data. (a) (2*S**)-3-Acetyl-5-[(*R**)-methylsulphinyl]-2-phenyl-2,3-dihydro-1,3,4-thiadiazole (**7a**); $C_{11}H_{12}N_2O_2S_2$, *M* = 268.348, monoclinic, *a* = 10.472(3), *b* = 14.170(4), *c* = 35.038(8) Å, β = 95.30(2)°, *V* = 5177.3(22) Å^3, *Z* = 16, D_C = 1.377 g cm^{-3}, *F*(000) = 2 240, μ = 4.0 cm^{-1}, space group *C*2/*c*.

(b) (1*R**,2*S**)-3-Acetyl-5-[(*S**)-methylsulphinyl]-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxide (**8b**); $C_{11}H_{12}N_2O_3S_2$, *M* = 284.347, orthorhombic, *a* = 17.141(2), *b* = 19.371(3), *c* = 7.721(1) Å, *V* = 2563.5(6) Å^3, *Z* = 8, D_C = 1.473 g cm^{-3}, *F*(000) = 1 184, μ = 4.2 cm^{-1}, space group *Pbca*. The structures of the two compounds were solved by direct methods using the MULTAN programs[9] and were refined by block-diagonal least-squares calculations with anistropic temperature factors for non-hydrogen atoms.

All hydrogen atoms were located from difference maps. Subsequent refinement was reached at *R* 0.042, R_w (w 1.0) 0.041 for compound (**7a**), and *R* 0.044, R_w (w 1.0) 0.041 for compound (**8b**). Then the hydrogen atoms were treated as isotropic. Atomic scattering factors used were taken from reference 10.

All crystallographic calculations were performed at the Data Processing Center in Kyoto University (MULTAN package), and on the PANAFACOM U-1400 computer in Tokushima Bunri University (X-STANP package). The anisotropic thermal parameters, the hydrogen co-ordinates and isotropic thermal parameters, and bond lengths involving hydrogen atoms have been deposited as a Supplementary Publication [SUP No. 56563 (5 pp.)].†

Acknowledgements

We thank Mrs. M. Ohe for elemental analyses, Mr. K. Kida for n.m.r. spectra, and Mrs. Y. Yoshioka for mass spectra. This work was supported in part by a grant from the Ministry of Education, Science and Culture, Japan.

† For details of the Supplementary Publications Scheme, see Instructions for Authors (1986), in *J. Chem. Soc., Perkin Trans. 1*, 1986, issue 1. Structure factors are available from the editorial office on request.

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Received 30*th July* 1985; *Paper* 5/1308