

**Methylation of 4-Phenyl-1,2,3-thiadiazole.
Reaction of Nucleophiles with *N*-Methyl-1,2,3-thiadiazolium
Salts and the Crystal Structure of the Products**

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The methylation of 4-phenyl-1,2,3-thiadiazole yields both *N*-methylated products. These react differently with nucleophiles. The structure of the product of the reaction with morpholine has been determined through X-ray diffraction analysis.

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Following studies of 1,2,3-thiadiazolium salts (1), we have investigated the methylation of 4-phenyl-1,2,3-thiadiazole with dimethyl sulfate. 4,5-Diphenyl-1,2,3-thiadiazole has been alkylated in low yield with methyl iodide (2) (several days heating under reflux in nitromethane), but the position of alkylation was not established. The use of methyl fluorosulphate increased the yield considerably, and through X-ray crystal structure determination the position of methylation was established as being at N(3) (3). However, treatment of 4-phenyl-1,2,3-thiadiazole I with dimethylsulphate in acetonitrile yielded mixture of both *N*-methylated products II and III in the ratio 1:2 (from the nmr spectrum of mixture). The salts II and III ($Y = ClO_4^-$) were easily separated because of the different solubility in acetic anhydride.

Reactions with Nucleophiles.

The 3-*N*-alkylated salt II was found to not react with morpholine. Treatment of II with methoxide ion at room temperature led to dealkylation of the salt; dithiafulvalene IV, being derived from the dealkylated compound (4) was also obtained. Further, treatment of II with methoxide ion at 0°, together with the above products, gave rise to 3-methyl-4-phenyl-1,2,3-thiadiazolium-5-thiolate V (5).

This product was also produced with triethylamine or ammonia in methanol; yields increased in the order: methoxide ion > triethylamine > ammonia.

The 2-*N*-alkylated salt III in methanolic solution with methoxide ion underwent dealkylation. Contrary to the reactivity of II, the salt III easily reacted with morpholine at room temperature to yield 2-methyl-4-phenyl-5-morpholino- Δ^3 -1,2,3-thiadiazoline VI. The thiadiazoline VI with mineral acids in methanolic solution returned to III at room temperature. The structure of VI was determined by 1H -nmr, ^{13}C -nmr and X-ray crystallographic analysis. The atomic fractional coordinates are reported in Table 1 and the structure of the molecule is shown in the Figure, together with bond lengths (Å) whose e.s.d.'s are 0.003 Å for bonds involving the sulphur atom and 0.006 Å for the others. Correction for rigid-body motion (6) did not

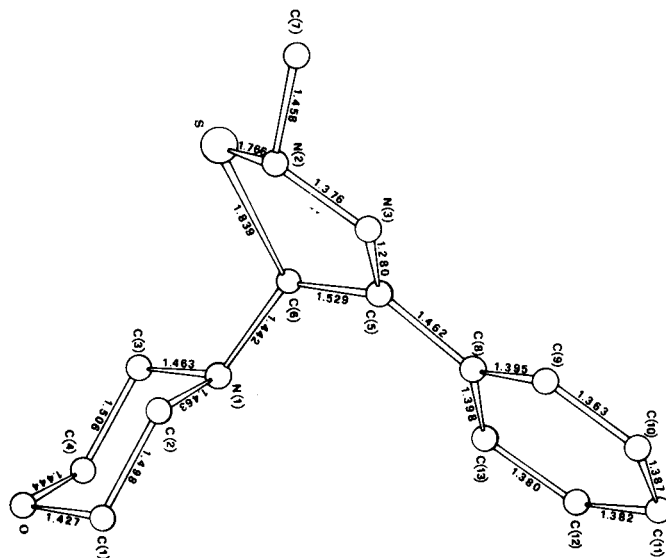
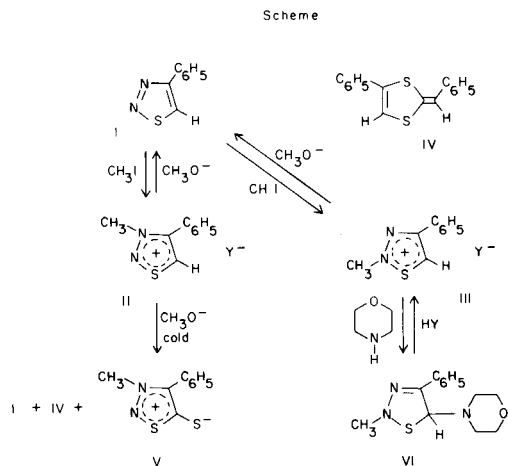


Figure: A perspective drawing of the molecule with the numbering scheme and bond distances. E.s.d.'s are 0.003 Å for distances involving the sulphur atom and 0.006 Å for the others.

significantly change bond distances (maximum deviation 0.003 Å). Four bond lengths in the five-membered ring compare well with expected values for single bonds, while N(3)-C(5) (1.28 Å) has the value of a >C=N- double bond.

In Table 2 we report the remaining relevant geometric data for the molecule. The five-membered ring is non-planar with the sulphur atom being displaced 0.491 Å from the least-squares plan passing through N(2), N(3), C(5) and C(6).

Table 1

Atomic Coordinates ($\times 10^4$) for Non-Hydrogen Atoms

	x	y	z
S	2354(1)	9329(1)	4522(2)
O	-1488(2)	7427(3)	1185(4)
N(1)	1072(2)	7151(3)	2630(4)
N(2)	2599(3)	8804(3)	7287(5)
N(3)	3060(2)	7432(3)	7410(5)
C(1)	-911(3)	6723(5)	3148(6)
C(2)	241(3)	7287(4)	4207(6)
C(3)	489(3)	7860(4)	598(6)
C(4)	-682(3)	7297(5)	-395(6)
C(5)	2903(3)	6751(3)	5549(5)
C(6)	2266(3)	7537(3)	3485(5)
C(7)	3362(4)	9672(4)	8810(7)
C(8)	3325(3)	5275(3)	5454(5)
C(9)	3902(3)	4592(3)	7373(6)
C(10)	4351(3)	3230(4)	7322(7)
C(11)	4220(3)	2487(4)	5308(7)
C(12)	3625(3)	3122(4)	3383(7)
C(13)	3181(3)	4504(4)	3446(6)

EXPERIMENTAL

Nmr spectra were determined with Varian Associates models 90 and XL 100; chemical shifts in δ ppm were measured with tetramethylsilane as internal standard. Mass spectra were taken on a "Hitachi-Perkin-Elmer" RMU 6D single focusing spectrometer. All melting points are uncorrected.

Methylation of 4-Phenyl-1,2,3-thiadiazole.

Dimethyl sulfate (37.8 g.) was added to 4-phenyl-1,2,3-thiadiazole (2) (16.4 g.) in acetonitrile (100 ml.) and the solution was heated under reflux for 8 hours. Perchloric acid (70%) (21 ml.) was added and the solid which separated was filtered, washed with acetonitrile and dried under vacuum. An nmr spectrum (DMSO- d_6) exhibited two methyl signals (δ 4.45 and 4.76) in the ratio 2:1. Extraction with hot acetic anhydride (200 ml.) yielded an insoluble residue of 3-methyl-4-phenyl-1,2,3-thiadiazolium perchlorate (II, Y = ClO $_4^-$), (7.8 g., yield 28%), m.p. 170° dec. (methanol); nmr (DMSO- d_6): δ ppm 9.93 (1H) s, 7.73 (5H) s, 4.44 (3H) s.

Anal. Calcd. for C $_9$ H $_9$ ClN $_2$ O $_4$ S: C, 43.46; H, 3.62; N, 11.26; S, 12.87. Found: C, 43.61; H, 4.01; N, 11.17; S, 13.08.

Cooling the filtrate yielded 2-methyl-4-phenyl-1,2,3-thiadiazolium perchlorate (III, Y = ClO $_4^-$) (16.8 g., yield 60%), m.p. 170° dec. (methanol); nmr (DMSO- d_6): δ ppm 10.17 (1H) s, 8.16-7.68 (5H) m, 4.77 (3H) s.

Anal. Calcd. for C $_9$ H $_9$ ClN $_2$ O $_4$ S: C, 43.46; H, 3.62; N, 11.26; S, 12.87. Found: C, 43.60; H, 3.91; N, 11.18; S, 13.02.

Reaction of *N*-Alkylated Products II and III with Methoxide Ion at Room Temperature.

Table 2
Geometric Data

Valence Angles (°). E.s.d.'s of all Angles are Smaller than 0.3°.

S - C(6) - N(1)	117.1	S - N(2) - N(3)	110.5
S - C(6) - C(5)	101.0	S - N(2) - C(7)	112.0
O - C(4) - C(3)	110.7	O - C(1) - C(2)	111.3
N(1) - C(6) - C(5)	112.1	N(1) - C(3) - C(4)	110.0
N(1) - C(2) - C(1)	109.5	N(2) - N(3) - C(5)	114.4
N(2) - S - C(6)	90.5	N(3) - C(5) - C(8)	120.0
N(3) - C(5) - C(6)	117.7	N(3) - N(2) - C(7)	112.1
C(8) - C(13) - C(12)	120.4	C(8) - C(9) - C(10)	122.1
C(8) - C(5) - C(6)	122.4	C(13) - C(12) - C(11)	120.2
C(13) - C(8) - C(9)	117.8	C(13) - C(8) - C(5)	121.4
C(12) - C(11) - C(10)	120.1	C(11) - C(10) - C(9)	119.3
C(9) - C(8) - C(5)	120.8		

Selected Torsion Angles (°).

S - N(2) - N(3) - C(5)	-18.3	N(2) - S - C(6) - C(5)	-19.7
C(7) - N(2) - N(3) - C(5)	-144.0	N(3) - C(5) - C(8) - C(9)	-0.1
N(2) - N(3) - C(5) - C(6)	-178.6	C(2) - N(1) - C(6) - C(5)	55.3

Least Squares Plane Through N(2), N(3), C(5) and C(6) (a).

$$-0.9152 X - 0.2119 Y + 0.3428 Z = 4.300$$

Deviations of Some Atoms from the Plane (Å).

S	-0.491	N(2)	0.003	N(3)	-0.006
C(5)	0.006	C(6)	-0.003	C(7)	-0.803
C(8)	0.029	N(1)	1.250		

Table 3

Crystal Data

Compound	SON $_3$ C $_9$ H $_9$ I $_7$
M $_r$	263.3
Crystal System	Triclinic
Cell Parameters	
a	11.30(3) Å
b	9.80(2)
c	6.14(2)
α	93.7°
β	101.2°
ν	82.2°
V	661.0 Å 3
D $_x$	1.32 Mg m $^{-3}$
F(000)	316
Space group	P1
μ (Mo K α)	0.236 mm $^{-1}$

Sodium methoxide (1.62 g.) in methanol (10 ml.) was added to II or III (2.78 g.) in methanol (20 ml.) at room temperature. The solution was filtered through celite, and the solvent was removed under reduced pressure to yield an oil, which, after column chromatography (dichloromethane) was shown to contain 4-phenyl-1,2,3-thiadiazole I [60% with II and 50% with III; m.p. 76-78°, lit. m.p. 77-78° (2)] and a small quantity of dithiafulvalene IV [9% with II and 12% with III; m.p. 127-128°, lit. m.p. 126-128° (4)].

Reaction of the 3*N*-Alkylated Product II with Methoxide Ion at Cold Temperature.

Sodium methoxide (1.1 g.) in methanol (10 ml.) was added to II (2.78 g.) in methanol (20 ml.) at 0°. The solvent was evaporated at cold

temperature. The remaining oil gave a crystalline compound on standing, which was recovered by filtration and recrystallized from chloroform or petroleum ether (0.5 g.), m.p. 140°. This compound is 3-methyl-4-phenyl-1,2,3-thiadiazolium-5-thiolate V (5); nmr (deuteriochloroform): δ ppm 7.55 (5H) s, 4.05 (3H) s; ms: M^+ cluster, m/e 207 (100), 208 (91), 209 (19), 210 (9).

Anal. Calcd. for $C_9H_8N_2S_2$: C, 51.89; H, 3.87; N, 13.45; S, 30.78. Found: C, 52.01; H, 3.83; N, 13.40; S, 30.66.

Reaction of the 2-N-Alkylated Product III with Morpholine.

Morpholine (1.84 g.) in methanol (10 ml.) was added dropwise to stirred 2-methyl-4-phenyl-1,2,3-thiadiazolium perchlorate III ($Y = ClO_4^-$) (2.78 g.) in methanol (30 ml.) at room temperature. After stirring (15 minutes) the mixture was diluted with water (50 ml.), the yellow residue was removed and after recrystallization from benzene yielded VI as yellow prisms (2.39 g., 91%), m.p. 96-98°; 1H -nmr (deuteriochloroform): δ ppm 8-7.2 (5H) m, 6.55 (1H) s, 3.68 (4H) t, 2.45 (4H) m, 3.20 (3H) s; ms: m/e 263 (M^+ 70), 177 (100); ^{13}C -nmr (DMSO- d_6): δ ppm 145.8 (N=C-C₆H₅), 131.2, 128.4, 128.2, 126.5 (6 aromatic carbon atoms), 87.4 (S-C-N), 65.5 (-CH₂-O-CH₂-), 47.6 (-CH₂-N-CH₂-), 45.3 (-CH₃).

Anal. Calcd. for $C_{13}H_{17}N_3OS$: C, 59.31; H, 6.84; N, 15.97; S, 12.16. Found: C, 59.50; H, 7.2; N, 15.91; S, 12.20.

X-Ray Data Collection.

Crystal data for the title compound are given in Table 3. The intensities of all reflections with $2\theta \leq 54^\circ$ (graphite monochromated Mo $K\alpha$ radiation) were measured on a Philips PW1100 automated four-circle diffractometer using the $\theta/2\theta$ scan technique (scan speed $0.05^\circ s^{-1}$, scan range 1.2°). For each reflection two background counts (8 s at each side of the peak) were averaged; two standard reflections, every hour, were measured to check the stability of the crystal and of the experimental

conditions. A total of 3157 independent reflections were recorded, of which 1590 having $I > \sigma(I)$ were considered observed. No absorption or extinction correction were applied.

Structure Solution and Refinement.

The structure was routinely solved with MULTAN 74 (7). The selected E-map revealed all but the hydrogen atoms, which have been subsequently located in a difference map. The refinement of all non-hydrogen atoms with anisotropic temperature factors was carried out by block-diagonal least-squares calculations. The final R value ($= \Sigma |F_o| - |F_c|/k / \Sigma |F_o|$) was 0.061 for the observed reflections. A table of observed and calculated structure factors may be obtained from the authors on request.

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