

Scheme 3

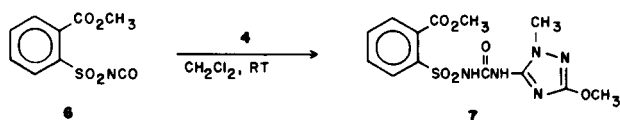


Table 1; bond distances and angles are shown in Tables 2 and 3.

Reaction of **1c** with methylhydrazine gave varying mixtures of **4** and **5** (predominantly **5**), from which **5** was obtained by recrystallization from ethanol. The methoxy protons of **4** and **5** resonate as singlets at 3.70 and 3.90 respectively in the pmr (DMSO- d_6).

In summary, the reaction of methylhydrazine with **1a** and **1c** predominantly involves displacement of the methylthio group by the more nucleophilic substituted nitrogen [9-12] and attack of the cyano function by the primary amine. This results in formation of the 3-aminotriazoles **2** and **5**. On the other hand, with **1b** the substituted nitrogen attacks the cyano function as opposed to displacing the methoxy group (which is displaced by the primary amine). As a result, the isomeric 5-aminotriazole **4** is obtained.

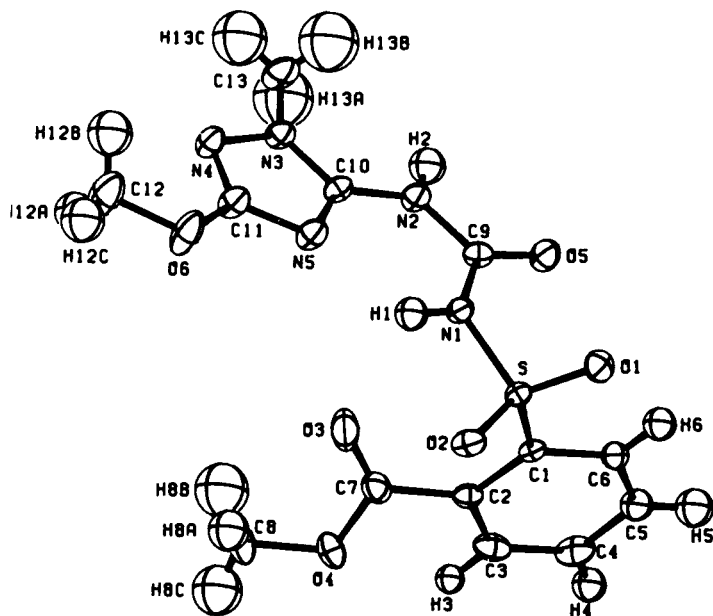


Figure 1. ORTEP Drawing of **7** showing the numbering of the atoms.

EXPERIMENTAL

Melting points were determined on a Thomas Hoover Unimelt apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 683 spectrophotometer in Nujol[®] mulls unless otherwise indicated. Pmr spectra were recorded on Varion EM360 and T-60 spectrometers in deuteriochloroform and DMSO- D_6 using tetramethylsilane as an internal reference. Elemental analyses were performed by the Agricultural Chemicals Department microanalytical section.

Table 1

Atomic Coordinates for Atoms in Crystalline **7** [a]

Atom	x	y	z
S	0.20895(5)	0.11329(4)	0.32608(8)
O1	0.2434(1)	0.2013(1)	0.3635(2)
O2	0.1304(1)	0.1030(1)	0.2046(2)
O3	0.1688(2)	-0.0877(1)	0.2702(3)
O4	0.0525(1)	-0.1488(1)	0.4215(3)
O5	0.4037(1)	0.0690(1)	0.4797(2)
O6	0.3197(1)	-0.1165(2)	-0.2534(2)
N1	0.3003(1)	0.0556(1)	0.2493(3)
N2	0.4448(2)	-0.0272(1)	0.2724(3)
N3	0.4917(1)	-0.1322(1)	0.0634(3)
N4	0.4584(2)	-0.1618(2)	-0.0937(3)
N5	0.3578(2)	-0.0549(2)	0.0088(3)
C1	0.1760(2)	0.0631(2)	0.5188(3)
C2	0.1291(2)	-0.0208(2)	0.5323(3)
C3	0.0950(2)	-0.0443(2)	0.6900(4)
C4	0.1102(2)	0.0100(2)	0.8295(3)
C5	0.1583(2)	0.0908(2)	0.8143(3)
C6	0.1900(2)	0.1172(2)	0.6589(3)
C7	0.1196(2)	-0.0867(2)	0.3922(4)
C8	0.0465(3)	-0.2207(2)	0.2992(5)
C9	0.3838(2)	0.0351(2)	0.3426(3)
C10	0.4314(2)	-0.0695(2)	0.1178(3)
C11	0.3791(2)	-0.1131(2)	-0.1161(3)
C12	0.3486(2)	-0.1801(2)	-0.3793(4)
C13	0.5810(2)	-0.1702(2)	0.1402(4)
H1	0.285(2)	0.022(2)	0.173(3)
H2	0.494(2)	0.043(2)	0.339(3)
H3	0.061(2)	0.098(2)	0.696(3)
H4	0.089(2)	-0.009(2)	0.937(3)
H5	0.168(2)	0.129(2)	0.911(3)
H6	0.222(2)	0.177(2)	0.647(3)
H8A	0.040(2)	-0.194(2)	0.185(4)
H8B	0.110(2)	-0.251(3)	0.292(4)

[a] Atoms are labelled in agreement with Figure 1. The numbers in parentheses are the estimated standard deviations in the last significant digit.

Dimethyl *N*-Cyanimidocarbonate (**1b**).

Following a procedure modeled after that of Wieland [6], 15.0 g (0.1 mole) of dimethyl *N*-cyanodithioimidocarbonate **1a** [7] was added to 750 ml of methanol followed by the addition of 1.0 g (19 mmoles) of sodium methoxide. The resulting clear solution was stirred at ambient temperature 48 hours. Concentrated hydrochloric acid (2.0 ml) was then added and the solvent was evaporated *in vacuo*, keeping the temperature below 40°. To the residue was added 400 ml of diethyl ether, and the resulting mixture was dried over magnesium sulfate, filtered, and evaporated to give a white solid. The crude product was suspended in cold diethyl ether, filtered and recrystallized directly from a minimal amount of diethyl ether to give 3.0 g (26% yield) of **1b**, mp 56-58° (after second recrystallization from diethyl ether), lit [6] mp 58-59°; pmr (deuteriochloroform): δ 4.0 (s, 6H, OCH₃); ir: 2200 (C≡N) cm⁻¹.

Dimethyl *N*-Cyanothioimidocarbonate (**1c**).

This compound was prepared by the procedure of Wieland [6], which in turn was based partly on the method of Hartke and Seib [13]. No attempt was made to isolate any of the intermediates in this sequence.

A methanol solution of sodium methoxide, prepared from 19.0 g (0.83 mole) of sodium and 650 ml of methanol, was added dropwise over one hour to a stirred solution of carbon disulfide (60.0 g, 0.78 mole) in 300 ml of methanol under nitrogen at 0°. The solution was then stirred at am-

bient temperature for 4 hours, concentrated to 300 ml to remove any remaining carbon disulfide, diluted with another 600 ml of methanol and cooled to 0°-5° while a solution of methyl iodide (112 g, 0.78 mole) in 105 ml of methanol was added over 25 minutes. The reaction was allowed to reach room temperature and stirred overnight.

The resulting methanolic solution of *O,S*-dimethylxanthate [14,15] was cooled to 0°, and a solution of cyanamide (33.3 g, 0.79 mole) and 85% potassium hydroxide (51.9 g, 0.78 mole) in 550 ml of methanol was added dropwise over one hour. After warming to room temperature and stirring 6 hours, the solution was again cooled to 0° and methyl iodide (112.5 g, 0.79 mole) was added dropwise followed by stirring at ambient temperature 15 hours [17]. The solution was concentrated (keeping the temperature below 40°), mixed with 700 ml of water, extracted with chloroform (4 × 300 ml), dried over magnesium sulfate and evaporated to give a yellow oil and a small amount of white solid. The solid was collected and washed with chloroform, giving 2.85 g of material (mp 200-202°) which was identified as 2-amino-4-methoxy-6-methylthio-1,3,5-triazine, lit [16] mp 197°; pmr (DMSO- D_6): δ 2.40 (s, 3H, SCH₃), 3.80 (s, 3H, OCH₃), 7.45 (broad s, NH₂); ir: 3370, 3300 3200, (NH₂), 1635 (C=N) cm⁻¹.

Removal of solvent from the filtrate *in vacuo* gave 36 g of oil which partially crystallized over 2 days at -20°. This solid was rapidly filtered, washed with cold diethyl ether, and dissolved in a minimal amount of boiling ether. At -20°, solid again precipitated; this was collected and washed with a small amount of cold diethyl ether and allowed to warm to room temperature, whereupon it melted. Traces of solvent were removed *in vacuo*, giving 17.4 g (17% overall yield based on carbon disulfide) of **1c** as a yellow oil. This material was used directly in the next step without further purification due to reported instability (6); pmr (deuteriochloroform): δ 2.55 (s, 3H, SCH₃), 4.05 (s, 3H, OCH₃); ir (neat): 2210 (C≡N), 1560 (C=N) cm⁻¹.

3-Methoxy-1-methyl-1H-1,2,4-triazol-5-amine (4).

To 1.2 g (10.5 mmoles) of **1b** stirring in 7 ml of acetonitrile at 0°, 0.9 ml (17 mmoles) of methylhydrazine was added dropwise. After stirring at 0° for 30 minutes, the reaction mixture was allowed to reach room temperature and stirred overnight; 1-chlorobutane (10 ml) was then added and the suspension stirred 10 minutes before filtering. The white solid was washed with 1-chlorobutane to yield 0.8 g of **4**. Removal of solvent from the filtrate gave an oily solid residue which was triturated in a small amount of acetonitrile/1-chlorobutane and filtered to give another 0.3 g of solid, bringing the combined yield to 82%. Recrystallization from acetonitrile gave a solid melting at 162-164°; pmr (DMSO- D_6): δ 3.35 (s, 3H, NCH₃), 3.70 (s, 3H, OCH₃), 6.20 (broad s, NH₂); ir: 3420, 3150 (NH₂), 1655 (C=N) cm⁻¹. A more satisfactory elemental analysis was not obtainable after repeated purification and reanalysis.

Anal. Calcd. for C₄H₈N₄O: C, 37.48; H, 6.29; N, 43.73. Found: C, 38.20; H, 6.20; N, 43.80.

A trace of the regioisomer **5** was observed by pmr in the above filtrate residue.

5-Methoxy-1-methyl-1H-1,2,4-triazol-3-amine (5).

Methylhydrazine (6.30 g, 0.136 mole) was added dropwise to a stirred solution of **1c** (17.3 g, 0.133 mole) in acetonitrile (35 ml) under nitrogen at 0°. When the resulting exotherm (temperature kept below 5°) was complete, the reaction mixture was allowed to warm to room temperature and stirred 48 hours. Filtration of the precipitate and washing with acetonitrile gave a white powder that was predominately regioisomer **5** (12.7 g, 75%). In repeating this experiment, the precipitate contained varying amounts of **4** and **5**; **5** could be isolated by recrystallization from ethanol: mp 178-180°; pmr (DMSO- D_6): δ 3.27 (s, 3H, NCH₃), 3.90 (s, 3H, OCH₃), 5.00 (broad s, NH₂); ir: 3320, 3200 (NH₂), 1650 (C=N) cm⁻¹.

Anal. Calcd. for C₄H₈N₄O: C, 37.49; H, 6.29; N, 43.73. Found: C, 37.90; H, 6.25; N, 43.20.

Table 2

Selected Bond Distances (Å) With Estimated Standard Deviations

C(1) - S	1.777(2)	S - O(1)	1.424(2)
S - N(1)	1.652(2)	S - O(2)	1.430(1)
N(1) - H(1)	0.808(024)	C(1) - C(2)	1.413(3)
N(1) - C(9)	1.377(3)	C(2) - C(7)	1.490(3)
C(9) - O(5)	1.224(2)	C(7) - O(3)	1.200(3)
C(9) - N(2)	1.380(3)	C(7) - O(4)	1.330(3)
N(2) - H(2)	0.880(024)	O(4) - C(8)	1.449(3)
N(2) - C(10)	1.389(3)	C(2) - C(3)	1.397(3)
C(10) - N(3)	1.330(3)	C(3) - C(4)	1.384(3)
N(3) - C(13)	1.463(3)	C(4) - C(5)	1.381(4)
N(3) - N(4)	1.389(2)	C(5) - C(6)	1.381(3)
N(4) - C(11)	1.314(3)	C(6) - C(1)	1.384(3)
C(11) - O(6)	1.3342(3)	C(8) - H8A	0.997(028)
O(6) - C(12)	1.444(3)	C(8) - H8B	0.978(032)
C(11) - N(5)	1.358(3)	C(8) - H8C	0.946(032)
N(5) - C(10)	1.326(3)	C(13) - H13A	0.866(038)
C(12) - H12A	0.994(028)	C(13) - H13B	0.922(039)
C(12) - H12B	0.986(028)	C(13) - H13C	0.868(035)
C(12) - H12C	0.966(028)	C(5) - H(5)	0.966(025)
C(3) - H(3)	0.930(022)	C(6) - H(6)	0.999(023)
C(4) - H(4)	0.961(023)		

Table 3

Selected Bonds Angles (Degrees) With Estimated Standard Deviations

C(1)-S-N(1)	108.40(9)	C(11)-O(6)-C(12)	114.7(2)
S-N(1)-H(1)	115(2)	C(11)-N(5)-C(10)	101.3(2)
S-N(1)-C(9)	122.8(2)	C(9)-N(1)-H(1)	116.7(2)
N(1)-C(9)-O(5)	123.0(2)	S-C(1)-C(2)	124.6(2)
N(2)-C(9)-O(5)	121.3(2)	C(1)-C(2)-C(7)	123.9(2)
C(9)-N(2)-H(2)	114(2)	C(2)-C(7)-O(3)	125.1(2)
C(9)-N(2)-C(10)	126.9(2)	C(2)-C(7)-O(4)	111.9(2)
C(10)-N(2)-H(2)	119(2)	O(3)-C(7)-O(4)	122.9(2)
N(2)-C(10)-N(5)	125.5(2)	C(7)-O(4)-C(8)	115.0(2)
N(2)-C(10)-N(3)	122.8(2)	O(2)-S-O(1)	118.5(1)
C(10)-N(3)-C(13)	131.1(2)	C(1)-S-O(1)	107.4(1)
N(4)-N(3)-C(13)	119.9(2)	C(1)-S-O(2)	109.36(9)
C(10)-N(3)-N(4)	109.1(2)	N(1)-S-O(1)	108.0(1)
N(3)-N(4)-C(11)	101.0(2)	N(1)-S-O(2)	104.80(9)
N(4)-C(11)-N(5)	116.8(2)	C(1)-C(2)-C(3)	117.2(2)
C(11)-N(5)-C(10)	101.3(2)	C(2)-C(3)-C(4)	121.8(2)
N(5)-C(10)-N(3)	111.7(2)	C(3)-C(4)-C(5)	120.1(2)
N(4)-C(11)-O(6)	124.4(2)	C(4)-C(5)-C(6)	119.5(2)
O(6)-C(11)-N(5)	118.7(2)	C(5)-C(6)-C(1)	121.0(2)
N(1)-C(9)-N(2)	115.7(2)	C(6)-C(1)-C(2)	120.5(2)

Methyl 2-[[[3-Methoxy-1-methyl-1H-1,2,4-triazol-5-yl]aminocarbonyl]aminosulfonyl]benzoate (7).

To a stirred suspension of **4** (0.6 g, 4.7 mmoles) in 8 ml of methylene chloride, 1.5 g (6.2 mmoles) of 2-carbomethoxybenzenesulfonyl isocyanate (**6**) [8] was added and the mixture stirred at room temperature overnight. The resulting white solid was collected and washed with methylene chloride to give 1.3 g (75% yield) of **7**, mp 177-179° (acetonitrile); pmr (DMSO- D_6): δ 3.50 (s, 3H, NCH₃), 3.83 (s, 3H, OCH₃), 3.90 (s, 3H, CO₂CH₃), 7.60-8.30 (m, 4H, ArH); ir: 1730, 1700 cm⁻¹.

Anal. Calcd. for C₁₃H₁₅N₅O₆S: C, 42.26; H, 4.10; N, 18.96. Found: C, 42.30; H, 4.10; N, 18.90.

Crystallographic Data and X-ray Structure Analysis of **7** [18].

Crystals of **7** are monoclinic, space group P2₁/c; a = 13.690 (2), b =

14.926 (2), c , 7.955 (1) Å; $\alpha = 90.00$ (1), $\beta = 91.85$ (1), and $\gamma = 90.00$ (1)°; $z = 4$; $d_c = 1.51$ g/cc. X-ray diffraction intensities were measured with a Syntex P3 diffractometer [Mok α radiation, $\lambda = 0.71069$ Å, graphite monochromator, 0-20 scan mode, $4^\circ < 2\theta < 55$, scan rate 4.0-10.0°/min., scan range 1.0°]. The total number of reflections measured was 3082, of which 2279 were used in the structure refinement.

The solution and refinement of the structure were carried out on a PDP-11 computer using local modifications of the programs supplied by the Enraf-Nonius Corp. [19].

The structure was solved by MULTAN [20] and refined by full-matrix least-squares methods to a final R factor of 4.0%. All hydrogen atoms were found from Fourier difference syntheses. The number of parameters refined in the last cycles was 286. The figure was produced by ORTEP [21].

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