N- and *C*-Sulfenylation of 1-(1,2-Oxazol-3 (and 5)-yl)-3-alkylureas with Organic Sulfenyl Chlorides

Kurt H. Pilgram* and Laird H. Gale

Biological Sciences Research Center, Shell Agricultural Chemical Company,
Modesto, California 95352

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Condensation of chlorocarbonylsulfenyl chloride **1** with 1-(5-(1,1-dimethylethyl)-1,2-oxazol-3-yl)-3-methylurea **4a** has been found to give isomeric 2,4-disubstituted-1,2,4-thiazolidine-3,5-diones **5** and **6**. Assignments are confirmed by the X-ray structure data of **6**. Sulfenylation with alkoxycarbonylsulfenyl chlorides **7** and trichloromethylsulfenyl chloride **10** of **4** occurs exclusively on N-1 rather than N-3 of the urea moiety. With the isomeric 1-[3-(1,1-dimethylethyl)-1,2-oxazol-5-yl]-3-methylurea **14** and ethoxycarbonylsulfenyl chloride **7b**, *C*-sulfenylated derivatives **15** and **16** are formed in low yield.

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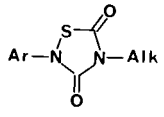
Introduction.

The results reported for the condensation of chlorocarbonylsulfenyl chloride **1** with a series of 1-alkyl-3-arylureas and 1-methyl-3-(5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl)-urea, which yielded **2** [1] and **3** [2], respectively, do not indicate the variability in the direction of cyclization that can occur in these reactions. For example, the reaction of **1** with 1-(5-(1,1-dimethylethyl)-1,2-oxazol-3-yl)-3-methylurea **4a** gave a mixture of isomeric 2,4-disubstituted-1,2,4-thiadiazolidine-3,5-diones, **5** and **6**. Of these, **6** showed exceptionally strong herbicidal properties [3]. Because their structure could not be unequivocally established from conventional spectroscopic analyses, we undertook the X-ray structure determination of **6**. In an attempt to prepare potential precursors of **6** unambiguously, the reactions of **4a** with alkoxycarbonylsulfenyl chlorides **7** and trichloromethylsulfenyl chloride **10** were investigated. The results are described below.



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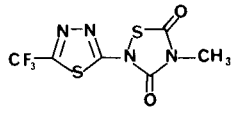

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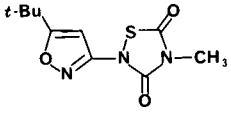

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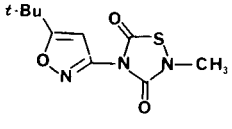

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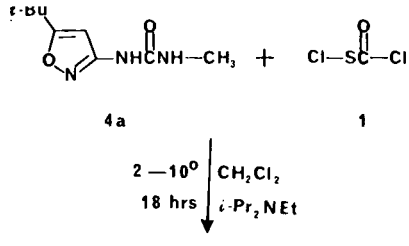
Results and Discussion.

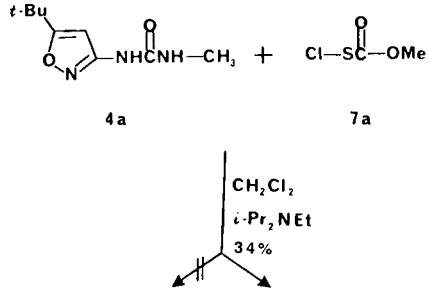
Isoxazol-3-ylureas.

Treatment of urea **4a** with chlorocarbonylsulfenyl chloride **1** in methylene chloride at 2-10°, followed by the dropwise addition of two molar equivalents of Hünig's base (ethyldiisopropylamine) lead to the formation and isolation in low yield of **5** and **6** (Scheme I), separated by silica chromatography techniques. In the presence of triethylamine, none of the product was formed. However, in every instance, considerable amounts of starting material **4a** were recovered.

Scheme I



Scheme II



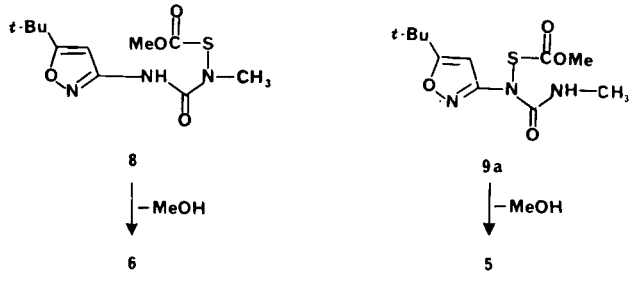
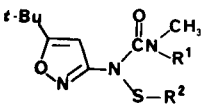


Table 1

Sulfenylated 5(and 3)-(1,1-Dimethylethyl)-1,2-Isoxazol-3(and 5)-yl-ureas



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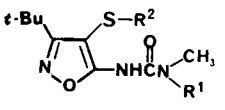

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No. of Compound	R_1	R_2	% Yield	Mp °C	Formula (Mol Weight)	Carbon Calcd. Found	Hydrogen Calcd. Found	Nitrogen Calcd. Found	^{1}H NMR Positions [a] for =CH	NH	NR_1 (R_1 = H)	ei-ms M^+
9a	H	CO_2CH_3	34	–	$C_{11}H_{17}N_3O_4S$ (287.34)	46.0 46.2	6.0 5.7	14.6 14.8	6.10	–	7.6	288 [b]
9b	H	$CO_2C_2H_5$	48	69-71	$C_{12}H_{19}N_3O_4S$ (301.35)	47.8 47.9	6.4 6.2	13.9 14.0	6.12	–	7.6	302 [b]
9c	H	$CO_2CH(CH_3)C_2H_5$	78	–	$C_{14}H_{23}N_3O_4S$ (329.41)	51.0 51.3	7.0 7.1	12.8 12.8	6.11	–	7.59	272 [c]
9d	H	$CO_2C(CH_3)_3$	12	–	$C_{14}H_{23}N_3O_4S$ (329.41)	51.0 51.1	7.0 7.0	12.8 12.4	6.11	–	7.59	330
9e	H	$CO_2CH(CH_3)C_6H_{13}$	43	–	$C_{18}H_{31}N_3O_4S$ (385.52)	56.1 55.8	8.1 7.8	10.9 10.8	6.38 [d]	–	7.55	386 [b]
9f	H	CCl_3	27	–	$C_{10}H_{14}Cl_3N_3O_2S$ (346.67)	34.6 34.2	4.1 3.9	12.1 11.8	6.23	–	7.55	346
9g	CH_3	CO_2CH_3	30	–	$C_{12}H_{19}N_3O_4S$ (301.36)	47.8 47.5	6.4 6.1	13.9 13.5	5.86	–	–	301
9h	CH_3	$CO_2CH(CH_3)C_2H_5$	11	–	$C_{15}H_{25}N_3O_4S$ (343.44)	52.5 52.6	7.3 7.7	12.2 11.9	5.85	–	–	343
9i	CH_3	CCl_3	36	105-108	$C_{11}H_{16}Cl_3N_3O_2S$ (360.70)	36.6 36.5	4.5 4.5	11.6 11.5	6.07	–	–	359
9j	OCH_3	CO_2CH_3	59	–	$C_{12}H_{19}N_3O_5S$ (317.36)	45.4 45.6	6.0 5.7	13.2 13.3	6.03	–	–	317
9k	OCH_3	CCl_3	55	–	$C_{11}H_{16}Cl_3N_3O_3S$ (376.70)	35.1 34.9	4.3 4.0	11.2 10.9	6.14	–	–	376
15a	H	$CO_2C_2H_5$	3	155-157	$C_{12}H_{19}N_3O_4S$ (301.35)	47.8 47.5	6.4 6.1	13.9 13.8	–	6.4	7.75	301
15b	H	$SCO_2C_2H_5$	3	123-126	$C_{12}H_{19}N_3O_4S_2$ [e] (333.42)	43.2 42.8	5.7 5.7	12.6 12.2	–	6.2	9.24	333
15c	H	$CO_2CH(CH_3)C_2H_5$	2	136-139	$C_{14}H_{23}N_3O_4S$ (329.41)	51.0 51.4	7.0 6.9	12.8 12.7	–	6.4	7.62	329

[a] δ (Deuteriochloroform) in ppm. [b] Ci-ms: $(MH)^+$. [c] M^+-Methylisocyanate. [d] DMSO-d_6. [e] Sulfur analysis, Calcd: S, 19.2. Found: S, 19.2.

Analytical (C, H, N) and spectral (ir, nmr, ms) data confirm the general formula of both **5** and **6**. However, the data do not permit unambiguous structure assignments. X-Ray structure analysis of **6** confirmed the original, tentative assignment.

In an attempt to prepare a potential precursor of **6**, namely **8**, **4a** was allowed to react with methoxycarbonylsulfenyl chloride **7a** in the presence of Hünig's base. Elimination from **8** of methanol could give **6**. However, none of the **8** compound was formed. Instead, its positional isomer **9a** which is a precursor of **5** was obtained in 34% by silica chromatography techniques (Scheme II). The mass spectral fragmentation pattern which shows a very prominent peak at m/z 230 (M^+-CH_3NCO) is in agreement with the assigned structure but does not support **8**.

Ethoxycarbonylsulfenyl chloride **7b** and its homologues reacted analogously with **4a** to give the respective **9** compounds (Table 1).

Trichloromethylsulfenyl chloride ("perchloromethyl mercaptan") **10** reacted analogously with the urea **4a** and the corresponding *N*,*N*-dimethyl- and *N*-methoxy-*N*-methylureas to give the respective *N*-(trichloromethylthio) derivatives **9f**, **9i**, **9k** in 27-55% yield (Table 1).

The analogous reaction of the propargyl urea **4b** with **10** in methylene chloride and in the presence of one molar equivalent of Hünig's base yielded the *N*-(trichloromethylthio) derivative **9l** (22%) in admixture with **11** (29%), rather than **12** resulting from the addition of **10** across the carbon-carbon triple bond (Scheme III). The structure of **9l** follows from its mass spectrum which shows the parent ion at m/z 412 (M^+) and strong peaks at m/z 290 (parent ion of **11**) and m/z 81 $(C(CH_3)_2C\equiv CCH_3)^+$. In addition, the ^1H nmr spectrum of **9l** has the expected proton count and positions for the assigned structure, *i.e.*, one signal for NH (δ 7.90), thus eliminating from consideration the structure of the addition product **12**.

The structure of **11** (m/z 290 (M^+)) has been confirmed by independent synthesis by reaction of 3-amino-5-(1,1-dimethylethyl)-1,2-oxazole **13** with **10**. Its formation from **4b** and **10** can be rationalized as proceeding *via* **13**. The intermediate formation of **13** from **4b** by loss of 1,1-dimethyl-2-butyn-1-yl isocyanate is not unexpected in view of the fact that almost all mono-alkyl ureas show the tendency to give off alkyl isocyanate, especially at elevated temperature [4,5].

Isoxazol-5-ylureas.

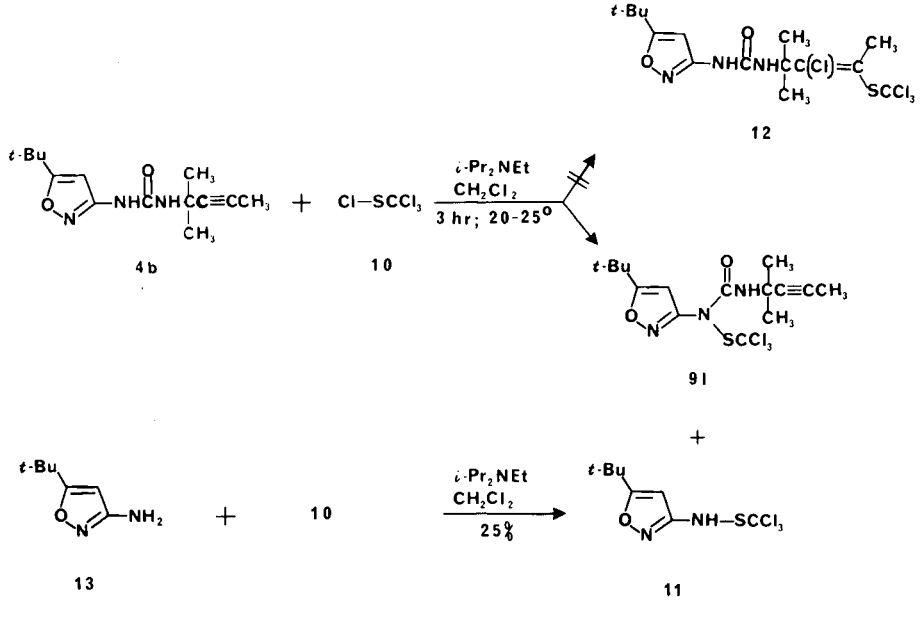
In an attempt to prepare similarly *N*-(alkoxycarbonylsulfenyl)ureas from the positionally isomeric isoxazolylurea **14** and **7b**, we observed *C*-sulfenylation rather than *N*-sulfenylation. For example, the reaction mixture obtained from the reaction of **14** with **7b** consisted of two compounds separated by silica chromatography. The first one was identified as the thiocarbonate **15a**; the second was characterized as the disulfide **15b** (Scheme IV).

The absence in the ^1H nmr spectra of **15a** and **15b** of the signals near 6.1 ppm characteristic of the olefinic =CH proton of the isoxazole ring, was instrumental in assigning structures. The behavior of **14** towards electrophilic substitution becomes plausible when viewed as the reaction of a typical enamine with an electrophile; enamines and tautomeric imines can be both *C*- and *N*-acylated.

X-Ray Crystallographic Analysis [6] of **6**.

A colorless plate crystal of **6** was grown from ethyl ether

Scheme III



Scheme IV

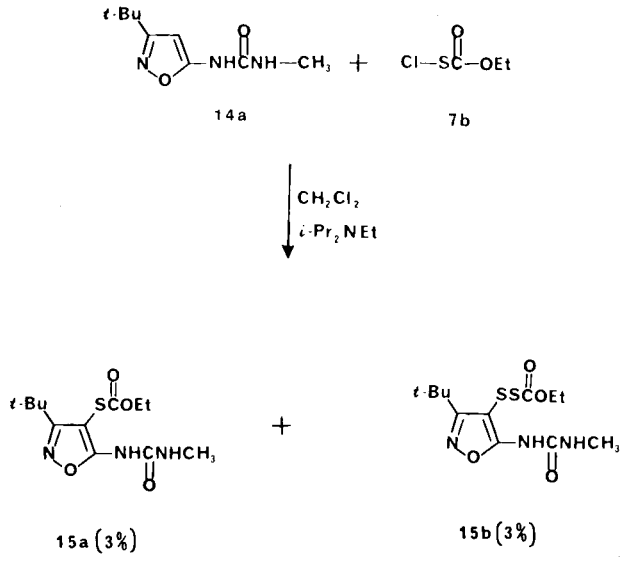


Table 2

Crystallographic Data

Molecular formula	$C_{10}H_{13}N_3O_3S$
Formula weight	255.30
Space Group	Monoclinic Cc
Linear absorption coefficient	23.2 cm^{-1}
Cell dimensions	a = 13.039 (1)Å b = 15.647 (3)Å c = 12.035 (1)Å β = 93.92 (1)° V = 2449.9 Å Z = 8
Calculated density (p)	1.38 g/cm^3
No. of reflections measured	2512
No. of unique reflections observed	2335

at room temperature with approximate dimensions of 0.40 x 0.20 x 0.08 mm. X-Ray intensities were measured on an Enraf-Nonius CAD4 computer controlled kappa axis diffractometer equipped with a graphite crystal incident beam monochromator. The data were collected at temperature of 23 ±1° using the W-θ scan technique. The scan rate varied from 2 to 2°/minute (in θ), depending on the intensity of the reflection. Data were collected to a maximum 2 of 140°. General information on the data collection and unit cell are given in Table 2. The structure was solved by direct methods and refined in the usual way (anisotropic temperature factors for non-hydrogen atoms, isotropic for hydrogen). The details of the structure solution and refinement are summarized in Table 3.

Crystals of **6** are monoclinic with space group Cc. The unit cell was found to consist of two unique molecules of the same structure in the space group Cc. The possibility of the central symmetric space group C2/c was examined and determined not to fit the structure. Details of the X-ray crystallographic analysis and unit cell are given in Table 2 and 3. An ORTEP plot of the X-ray crystallographic structures of the two unique molecules in a unit cell of **6** are shown in Figures 1 and 2. The unit cell packing structure and stereoscopic view of the unit cell, with one-half of the molecules removed for clarity, are shown in Figures 3 and 4. The bond distances, bond angles, and torsional angles for each crystallographically unique molecule in a unit cell are listed in Table 4, 5, and 6.

Table 3

Structure Solution and Refinement

Solution:	Direct methods
Hydrogen atoms:	Refined with Biso = 5.0A^3
Refinement:	Full-matrix least-squares
Minimization function:	$\Sigma w(\mid Fo \mid - \mid Fc \mid)^2$
Least-squares weights:	$4Fo^2 / \sigma^2(Fo^2)$
"Ignorance" factor:	0.050
Anomalous dispersion:	All non-hydrogen atoms
Reflections included:	1900 with $Fo^2 > 3.0\sigma(Fo^2)$
Parameters refined:	384
Unweighted agreement factor:	0.037
Weighted agreement factor:	0.046
Factor including unobs data:	0.068
Esd of obs of unit weight:	1.34
Convergence, largest shift:	0.50σ
High peak in final diff map:	0.20 (4) e/A^3
Computer hardware/software:	POP-11/60 based TEXRAY system

Table 4

Selected Bond Distances in Angstroms

Atom 1	Atom 2	Molecule 1	Molecule 2
S1	N2	1.706 (3)	1.689 (4)
S1	C1	1.752 (4)	1.749 (4)
O1	C1	1.205 (5)	1.200 (5)
N1	C1	1.376 (5)	1.372 (5)
N1	C2	1.394 (5)	1.410 (5)
O2	C2	1.200 (5)	1.207 (4)
N2	C2	1.354 (5)	1.343 (5)
N2	C4	1.433 (6)	1.444 (6)
N1	C3	1.411 (4)	1.403 (5)
N3	C3	1.298 (4)	1.298 (5)
C3	C5	1.402 (5)	1.407 (5)
C5	C6	1.361 (5)	1.334 (5)
C6	C7	1.499 (5)	1.497 (5)
C6	O3	1.351 (4)	1.351 (4)
N3	O3	1.398 (4)	1.395 (4)

Numbers in parentheses are estimated standard deviations in the least significant digits.

Table 5

Selected Bond Angles in Degrees

Atom 1	Atom 2	Atom 3	Molecule 1	Molecule 2
N2	S1	C1	91.0 (2)	91.1 (2)
S1	C1	N1	108.0 (3)	108.1 (3)
S1	C1	O1	125.3 (3)	124.6 (3)
N1	C1	O1	126.7 (4)	127.2 (4)
C1	N1	C2	116.7 (3)	116.2 (3)
N1	C2	N1	109.4 (3)	109.0 (3)
N1	C2	O2	124.4 (3)	124.7 (4)
O2	C2	N2	126.2 (4)	126.3 (4)
C2	N2	S1	114.6 (3)	115.5 (3)
C2	N2	C4	124.6 (4)	122.4 (4)
S1	N2	C4	120.1 (3)	121.3 (4)
N1	C3	N3	118.5 (3)	119.2 (3)
N1	C3	C5	127.5 (3)	128.4 (3)
C3	N3	O3	104.0 (3)	104.5 (3)
N3	O3	C6	109.6 (3)	109.6 (3)
O3	C6	C7	116.6 (3)	116.5 (3)
C5	C6	C7	134.3 (3)	134.7 (4)
O3	C6	C5	109.1 (3)	108.8 (3)
C6	C5	C3	103.2 (3)	104.8 (3)
C5	C3	N3	114.0 (3)	112.4 (3)

Numbers in parentheses are estimated standard deviations in the least significant digits.

Table 6

Selected Torsional Angles in Degrees

Atom 1	Atom 2	Atom 3	Atom 4	Molecule 1	Molecule 2
C2	N1	C3	C5	54.3	130.5
C2	N1	C3	N3	−126.0	−51.5
C1	N1	C3	C5	−120.7	−40.7
C1	N1	C3	N3	59.0	129.3

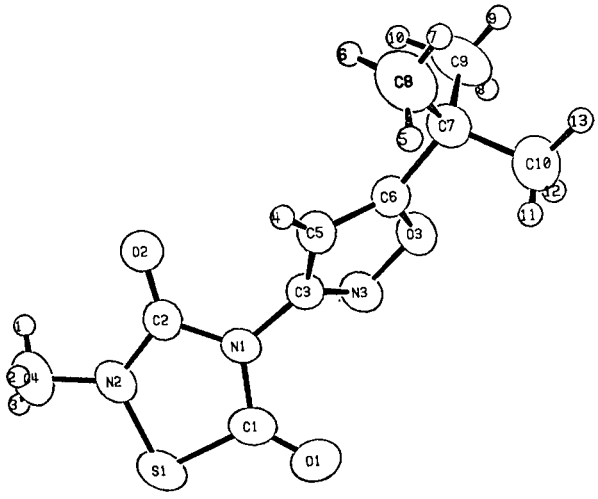


Figure 1. ORTEP Plot of X-Ray Crystallographic Structure of **6**. Conformation 1.

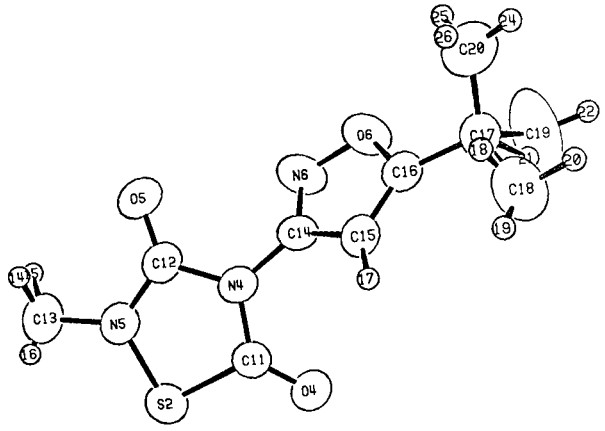


Figure 2. ORTEP Plot of X-Ray Crystallographic Structure of **6**. Conformation 2.

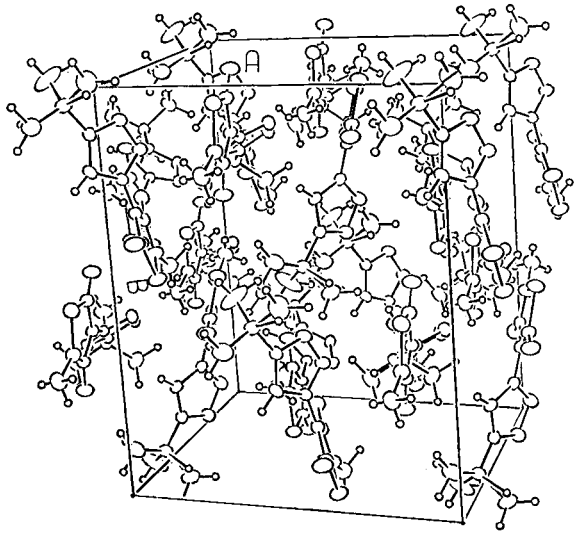


Figure 3. Unit Cell of **6**.

These data clearly show that the heterocyclic ring containing the sulfur atom is a five-membered rather than a seven-membered ring. Furthermore **6** is the isomer where the substituents on the 1,2,4-thiadiazolidine-3,5-dione ring are the methyl group on the 2-nitrogen and the *t*-butylisoxazole moiety on the 4-nitrogen atom. As would be expected, each five-membered ring in the molecule is essentially planar. The principal difference between the two crystallographically unique molecules in a unit cell is the dihedral angle between the two planar five-membered rings (see Table 6). This is shown more clearly by Newman projections of the nitrogen-carbon bond connecting the two five-membered rings for the two conformations (see Figure 5). In conformation 1, the dihedral angle between the two five-membered rings is 54.3°, while in conformation 2, this angle is increased to 130.5°.

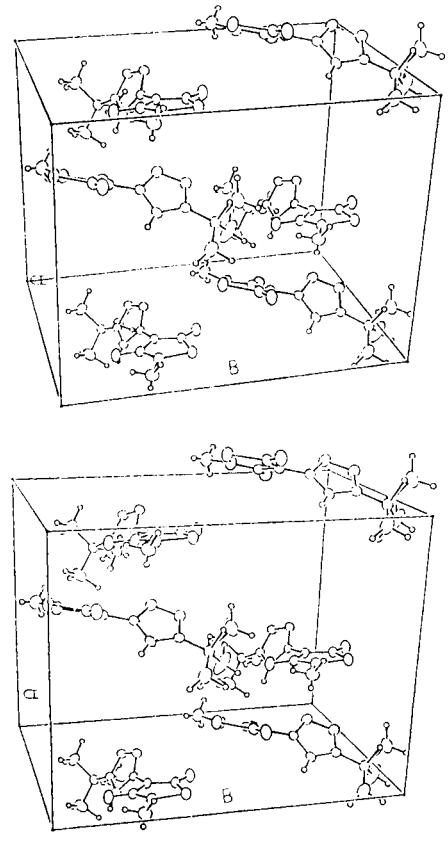


Figure 4. Stereoscopic View of Unit Cell of **6** (One-half of Molecules Removed).

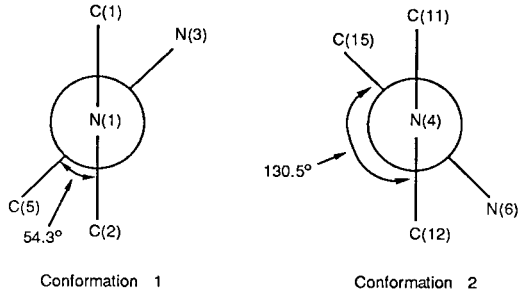


Figure 5. Newman Projection N(1)-C(3) Bond.

EXPERIMENTAL

General Methods.

Melting and boiling points are uncorrected. The ^{1}H nmr spectra were recorded at 60 MHz on a Varian EM-360 spectrometer with tetramethylsilane as an internal standard. Electron inpact mass spectra were determined at 70 eV on a Finnigan 3200 mass spectrometer by direct introduction *via* solid probe. Chemical ionization mass spectra were obtained at 70 eV on a Finnigan 4000 mass spectrometer. A Finnigan 6110 Data System was used for data acquisition.

Alkoxycarbonylsulfenyl chlorides **7** were prepared according to published methods. The first consists of the reaction of **1** with an alcohol [7]. This method gave good yields of **7a** and **7b**. For the alkoxycarbonylsulfenyl chlorides derived from isopropyl alcohol, 2-butanol, and 2-octanol, we applied the cleavage by chlorine of unsymmetrical diacyl sulfides [8]. 3-Amino-5-(1,1-dimethylethyl)-1,2-oxazole (**13**) [9,10] and ureas **4** [9,10] and **14** [11], were prepared according to published methods.

4-Methyl-2-[5-(1,1-dimethylethyl)-1,2-oxazol-3-yl]-1,2,4-thiadiazolidine-3,5-dione (**5**), and 2-Methyl-4-[5-(1,1-dimethylethyl)-1,2-oxazol-3-yl]-1,2,4-thiadiazolidine-3,5-dione (**6**).

To a clear solution containing 220.9 g (1.12 moles) of **4a** and 176.9 g (1.35 moles) of chlorocarbonylsulfenyl chloride (**1**) in 3,000 ml of methylene chloride was added dropwise with stirring at 2° a solution of 289.0 g (2.24 moles) of ethyldiisopropylamine in 600 ml of methylene chloride. This addition was slow and was extended to 7 hours. The reaction mixture was packed in ice and left standing for 18 hours. The reaction mixture was poured into 4000 ml of ice water and phase separated. The methylene chloride layer was dried (magnesium sulfate) and concentrated under rotary evaporation. The residue was purified by silica chromatography [solvent No. 2 [12] and No. 3 [12] (1:1)].

The first fraction consisted of 64.0 g (29%) of starting material **4a**.

The second fraction consisted of 6.6 g (2%) of tan solid **5**, mp 114-116° (from ether); ir (potassium bromide): no OH, NH, 1736, 1694 (C=O), 1600-1500 (C=, C=N) cm^{-1}; ei/ms: (m/z) 255 (M^+), 240 (M^+-CH_3), 170 (M^+-$CH_3N(CO)_2$); ^{1}H nmr (deuteriochloroform): δ 1.38 (9H, $(CH_3)_3C$), 3.26 (3H, NCH_3), 6.26 (1H, =CH).

Anal. Calcd. for $C_{10}H_{13}N_3O_3S$ (255.29): C, 47.0; H, 5.1; N, 16.5. Found: C, 46.9; H, 5.2; N, 16.1.

The third fraction consisted of 26.4 g (9%) of tan solid **6**, mp 113-115°; ir (potassium bromide): 3136 (=CH), 1753, 1696 (C=O), 1645 (C=C), 1591 (C=N), 1360 (-CH_3) cm^{-1}; ei/ms: (m/z) 255 (M^+), 240 (M^+-CH_3), 198, 151, 141, 135, 123, 89, 61, 57, 41; ^{1}H nmr (deuteriochloroform): δ 1.38 (9H, $(CH_3)_3C$), 3.26 (3H, NCH_3), 6.26 (1H, =CH).

Anal. Calcd. for $C_{10}H_{13}N_3O_3S$ (255.29): C, 47.0; H, 5.1; N, 16.5. Found: C, 47.0; H, 5.2; N, 16.4.

1-Methyl-3-[5-(1,1-dimethylethyl)-1,2-oxazol-3-yl)-3-(methoxycarbonylthio]-urea (**9a**).

Compound **7a**, 15.2 g (0.12 mole), was added to a stirred solution of 20.0 g (0.1 mole) of **4a** in 500 ml of chloroform, then 12.1 g (0.12 mole) of triethylamine was added dropwise, all at 10-15°. The mixture was stirred at room temperature for 2 hours, briefly warmed to reflux temperature, then stirred at room temperature for 4 hours, poured into ice water, and the two phases were separated. The chloroform layer was washed with water, dried (magnesium sulfate), filtered and concentrated to dryness. The residue was crystallized from ether; the crystals were separated, and the mother liquor was chromatographed on silica gel using solvent No. 2 [12] as eluent to give 9.7 g (34%) of **9a** as an amber syrup; ir (methylene chloride): *ca.* 3600 (trace -OH), 3437, 3323 (-NH), 3000-2800 (-CH), 1709 (C=O, urea), 1744 (C=O, thiocarbonate), 1518 (C=N), 1200-1000 (C-OC), 1555 (CONH) cm^{-1}; ei/ms: (m/z) 288 (MH^+), 272 (M^+-CH_3), 262 (M^+-CH_3OH), 255, 230 (M^+-CH_3NCO), 171, 140 (parent amine$^+$), 129, 125 (m/z 140-CH_3), 89, 68, 57 (CH_3NCO^+).

1-(1,1-Dimethyl-2-butyn-1-yl)-3-[5-(1,1-dimethylethyl)-1,2-oxazol-3-yl]-3-(trichloromethylthio)urea (**9l**) and 5-(1,1-Dimethylethyl)-3-[(trichloromethylthio)amino]-1,2-oxazole (**11**).

To a stirred solution of 5.2 g (0.02 mole) of **4b** in 250 ml of methylene chloride was added 4.1 g (0.022 mole) of **10** followed by the slow addition of 5.16 g (0.04 mole) of Hünig's base. After 3 hours at room temperature, the reaction mixture was poured into ice water and phase separated. The organic layer was dried (magnesium sulfate), concentrated under rotary evaporation, adsorbed on silica gel, and purified by using solvent No. 1 [12] as eluent.

The first fraction consisted of 1.7 g (29%) of **11**, mp 137-139°; ir (potassium bromide): *ca.* 3200 (-NH), 3000-2800 (-CH), 1611 (C=), 1472 (C=N), 800-700 (-Cl) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.31 (9H, $(CH_3)_3C$), 6.01 (1H, =CH), 7.41 (1H, NH); ei/ms (m/z): 290 (M^+), 254

(M^+-Cl), 171 (ArNHS$^+$), 118 (CCl_3^+), 79, 57 ($C_4H_9^+$), 41.

Anal. Calcd. for $C_6H_{11}Cl_3N_2OS$ (289.63): C, 33.2; H, 3.8; N, 9.7. Found: C, 33.6; H, 3.9; N, 9.4.

The second fraction consisted of 1.8 g (22%) of amber liquid **9l**, ir (methylene chloride): 3414, *ca.* 3300 (-NH), 3000-2800 (-CH), 1726 (C=O), 1661 (C=C), 1537 (-CONH), 1600-1400 (ring); ^{1}H nmr (deuteriochloroform): δ 1.34 (9H, $(CH_3)_3C$), 1.66 (6H, $(CH_3)_2C$), 1.81 (3H, CH_3C), 6.26 (1H, =CH), 7.90 (1H, NH); ei/ms (m/z): 412 (M^+), 397 (M^+-CH_3), 376 (M^+-Cl), 290 (**11**$^+$), 253 (m/z 388-Cl), 171, 118 (CCl_3^+), 81 ($(CH_3)_2CC{\equiv}CCH_3^+$), 57 ($C_4H_9^+$).

Anal. Calcd. for $C_{15}H_{20}Cl_3N_3O_2S$ (412.76): C, 43.6; H, 4.9; N, 10.2. Found: C, 43.9; H, 4.5; N, 9.8.

1-[4-(Ethoxycarbonylthio)-3-(1,1-dimethylethyl)-1,2-oxazol-5-yl]-3-methylurea (**15a**) and 1-[4-(Ethoxycarbonyldithio)-3-(1,1-dimethylethyl)-1,2-oxazol-5-yl]-3-methyl)urea (**15b**).

To a stirred solution of 10.0 g (0.051 mole) of (**14**) in 375 ml of methylene chloride was added 10.4 g (0.074 mole) of (**7b**), followed by the dropwise addition of 9.5 g (0.074 mole) of diisopropylethylamine. After 2 hours, the reaction mixture was diluted with 700 ml of ice water, acidified with dilute hydrochloric acid, phase-separated, dried (magnesium sulfate), and concentrated under rotary evaporation. The residual resin, 10.1 g, was purified by silica chromatography (Solvent system No. 3 [12]). Two fractions were collected and recrystallized from ether.

The first fraction consisted of 0.5 g (3%) solid **15b**, mp 123-126°; ir (methylene chloride): 3456-3200 (-NH), 3000-2800 (-CH), 1713 (C=O), 1599 (C=C), 1177, 1152 (C-OC); ei/ms: (m/z) 333 (M^+), 276 (M^+-CH_3NCO), 260 (M^+-$CO_2C_2H_5$), 203 (m/z 260-CH_3NCO), 57 (CH_3NCO^+).

The second fraction consisted of 0.5 g (3%) of solid **15a**, mp 155-157°; ir (methylene chloride): 3455, 3379 (-NH), 3000-2800 (-CH), 1734-1688 (C=O), 1600 (C=C), 1543 (CONH); ei/ms: (m/z) 301 (M^+), 244 (M^+-CH_3NCO) 228 (M^+-$CO_2C_2H_5$), 172 (M^+-$CO_2C_{21}H_5$, CH_3NCO), 146, 89, 57 (CH_3NCO^+).

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Supplementary Material Available.

Complete X-ray data on compound **6** are available upon request from the author (KHP) including tables of fractional atomic coordinates for non-hydrogen atoms, thermal parameters, bond lengths, bond angles, intermolecular contacts, mean planes, and torsion angles (21 pages).

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[12] Solvent system No. 1 (by volume): tetrahydrofuran (4), hexane (96); No. 2: tetrahydrofuran (4), ethyl acetate (16), hexane (80); No. 3: tetrahydrofuran (4), ethyl acetate (30), hexane (66).