Photodegradation of a 1,3,4-Thiadiazole-urea Herbicide. Isolation, Characterization, X-Ray Crystal Structure and Synthesis of Photoproducts

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The photodegradation of 1,3-dimethyl-1-(2-(3-fluorobenzylthio)-1,3,4-thiadiazol-5-yl)urea as a thin film and in solution is described. The two photoproducts from thin-film photolysis were characterized by spectral and synthetic methods. The X-ray crystal structure of one of the photoproducts is also reported. The rearrangements were shown to involve an *S*-to-*N* benzyl migration, followed by a sulfur-oxygen substitution.

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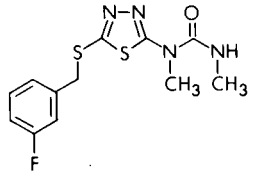
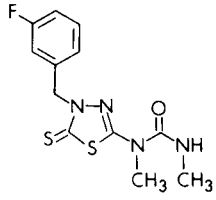
The photostability of agricultural agents is a problem of growing interest, prompting the publication of a number of reviews [3] which point to the importance of this transformation pathway. As part of a program aimed at discerning the mechanism of selectivity [4] of 1,3-dimethyl-1-(2-(3-fluorobenzylthio)-1,3,4-thiadiazol-5-yl)urea **1**, we have examined the photolysis of **1** on glass plates and in solution. Here we report the isolation and characterization by spectral and synthetic methods of the two photoproducts, formed sequentially under the conditions of thin-film photolysis.



1



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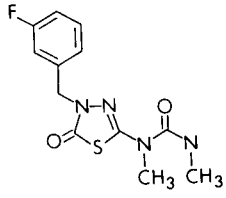

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Results and Discussion.

Compound **1** was found to be rapidly degraded when exposed to sunlight as a thin film on glass. A similar degradation pattern was found when a solution of **1** in methylene chloride was exposed to ultraviolet light. The photochemical half-life of **1** in solution was found to be approximately 1.3 hours as determined by both pmr and reverse-phase hplc (data not shown).

The thin-film photolysis of **1** was found to afford two products, isolated by a series of preparative layer chromatograms. The less polar of these products, **2**, could also be prepared under the conditions of solution photolysis in 40% isolated yield. This material was characterized by a combination of spectral techniques. The mass spectrum suggested that **2** was isomeric with **1** having essentially the same fragmentation pattern with minor changes in the relative intensity of the ions at m/z 255 and 166. Compound **2** also displayed an increased tendency to form a methylisocyanate cation (m/z 57) rather than the methylaminocarbonyl cation (m/z 58). The isomeric nature of **1** and **2** was confirmed by elemental analysis. The infrared spectrum failed to shed any light on the identity of **2**, only confirming the presence of the urea carbonyl, a 1,3-substitution pattern on the aromatic ring, and an N-H moiety.

The pmr of **2** showed a prominent downfield shift of the benzylic methylene from δ 4.37 to δ 5.42 and an upfield shift of the methyl group on the nitrogen adjacent to the 1,3,4-thiadiazole ring from δ 3.57 to δ 3.30. These results suggested some modification of the thiadiazole ring, but failed to clearly define the nature of the modification. At least three possible rearrangement products were hypothesized (Scheme 1), two of which would involve diazirine intermediates similar to the thiophene photorearrangements previously described by Wynberg [5]. The third possibility (C) would represent an *S*-to-*N* migration of the fluorobenzyl group, analogous to the rearrangement of 4-benzyl-1-methyl-pyrimidin-2-one described by Fourrey and Jouin [6].

To further elucidate the nature of **2**, [^{13}C]-labeled-**1** was prepared from [^{13}C]-carbon disulfide (Scheme 2). The ^{13}C-nmr spectrum of this material and its photolysis product clearly indicated a significant alteration of the environment at C-2 of the thiadiazole ring. Although we felt confident in removing possibility A from further consideration, we were still faced with at least two possibilities. The structure of **2** was ultimately determined by X-ray crystallography, showing the rearrangement to involve the

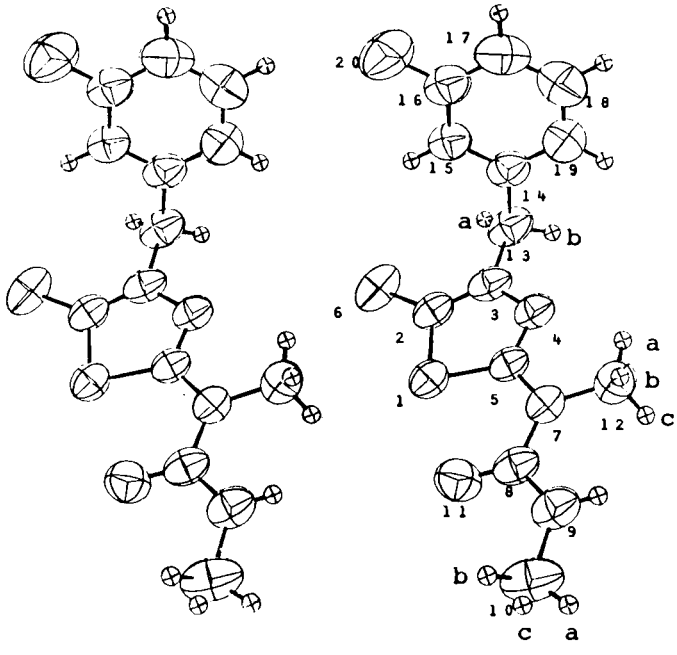


Figure 1. Stereoscopic View of Compound **2**.

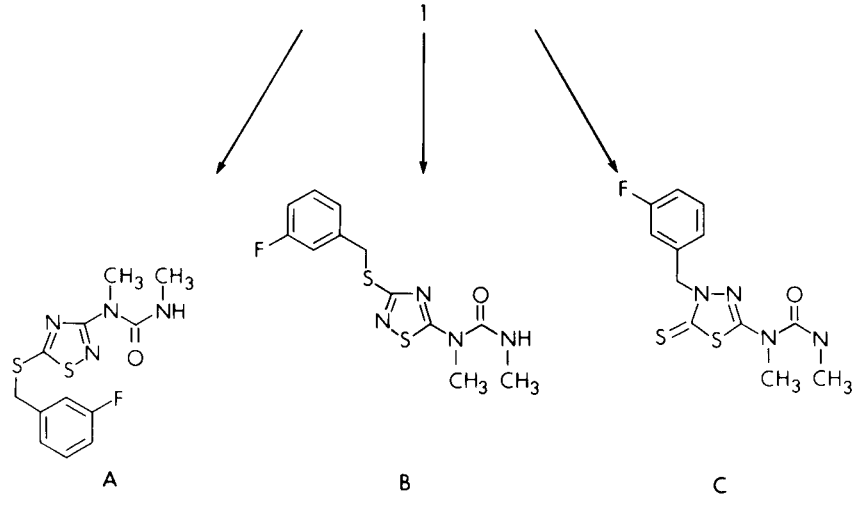
proposed benzyl-migration and accounting for the downfield shift of the benzylic methylene in the pmr by the anisotropic effect of the thiocarbonyl [7]. The atomic coordinates and molecular dimensions of **2** are given in Tables 1 and 2, respectively.

Having determined the structure of **2**, the characterization of **3** was rather straight-forward. Exposing a thin film of **2** to sunlight was found to provide **3** quantitavely, indicating the sequential nature of their formation. The mass spectrum and elemental analysis of **3** suggested that one of the sulfur atoms of **2** had been replaced by oxygen. The in-

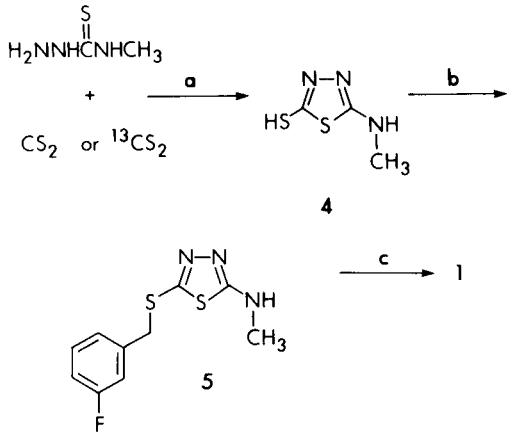
Table 1

Atomic Coordinates Expressed as Fractions of the Unit Cell Axes

Atom	X	Y	Z
S(1)	0.11565(6)	0.1428(1)	0.08342(5)
S(6)	0.19331(8)	-0.0787(1)	0.25649(6)
F(20)	0.0893(2)	0.2973(3)	0.5519(1)
O(11)	0.0833(1)	0.3153(2)	-0.0734(1)
N(3)	-0.0014(2)	0.0375(3)	0.1909(2)
N(4)	-0.0684(2)	0.1297(3)	0.1223(1)
N(7)	-0.0662(2)	0.2878(3)	-0.0153(1)
N(9)	-0.06919(2)	0.4370(3)	-0.1566(2)
C(2)	0.0992(2)	0.0278(3)	0.1842(2)
C(5)	-0.0168(2)	0.1918(3)	0.0608(2)
C(8)	-0.0094(2)	0.3462(3)	-0.0835(2)
C(10)	-0.0121(3)	0.4972(4)	-0.2343(2)
C(12)	-0.1777(2)	0.3223(4)	-0.0219(2)
C(13)	-0.0478(3)	-0.0358(4)	0.2680(2)
C(14)	-0.0640(2)	0.0828(4)	0.3449(2)
C(15)	0.0206(2)	0.1373(4)	0.4133(2)
C(16)	0.0048(3)	0.2460(4)	0.4822(2)
C(17)	-0.0895(3)	0.3024(5)	0.4872(2)
C(18)	-0.1742(3)	0.2476(6)	0.4200(3)
C(19)	-0.1617(3)	0.1382(5)	0.3488(3)
H(9)	-0.126(2)	0.448(3)	-0.161(1)
H(10a)	-0.060(0)	0.559(0)	-0.279(0)
H(10b)	0.047(0)	0.561(0)	-0.204(0)
H(10c)	0.012(0)	0.411(0)	-0.268(0)
H(10d)	0.061(0)	0.474(0)	-0.217(0)
H(10e)	-0.042(0)	0.449(0)	-0.295(0)
H(10f)	-0.021(0)	0.608(0)	-0.239(0)
H(12a)	-0.200(0)	0.271(0)	0.031(0)
H(12b)	-0.186(0)	0.434(0)	-0.017(0)
H(12c)	-0.217(0)	0.286(0)	-0.084(0)
H(13a)	-0.003(0)	-0.118(0)	0.301(0)
H(13b)	-0.114(0)	-0.082(0)	0.238(0)
H(15)	0.090(0)	0.105(0)	0.411(0)
H(17)	-0.097(0)	0.380(0)	0.536(0)
H(18)	-0.243(0)	0.282(0)	0.423(0)
H(19)	-0.221(0)	0.105(0)	0.301(0)

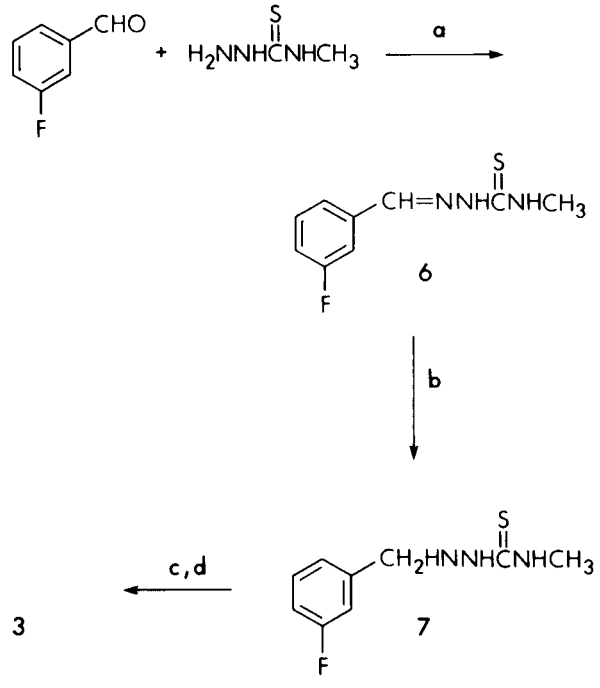


Scheme 1. Hypothesized Structures for Photorearrangement Product of **1**.



Scheme 2. Synthesis of Compound **1**. [a] Dimethylformamide, reflux. [b] 2 *N* Potassium hydroxide, 3-fluorobenzyl chloride, methanol. [c] Methylene chloride 1,4-diazobicyclo[2.2.2]octane, methylisocyanate.

frared spectrum showed the presence of two carbonyl groups (1672 and 1647 cm^{-1}), consistent with structure **3**. The final structure proof was completed by total synthesis (Scheme 3), following the general procedures described by Sasse [8] for other (4-substituted-1,3,4-thiadiazolin-5-one-2-yl)ureas.



Scheme 3. Synthesis of Compound **3**. [a] Ethanol, reflux. [b] Sodium borohydride; ethylene glycol monomethyl ether, reflux. [c] Phosgene, chloroform, toluene, reflux. [d] Methylamine, diethyl ether.

While it was clear that the transformation of **1** to **2** is a photochemical process, the nature of the transformation of **2** to **3** was not so obvious. To examine the possibility of simple hydrolysis of the thiocarbonyl, **2** was subjected to a variety of conditions. Refluxing in water (*p*H 5.6) or in 1 *N* hydrochloric acid for 48 hours resulted in no detectable change of **2**. In a similar manner, stirring **2** in a 3:8 mixture of ethanol and 2 *N* sodium hydroxide for 48 hours at room temperature resulted in no modification of the molecule. By refluxing the basic solution, hydrolysis of the urea moiety with no detectable alteration of the thiocarbonyl could be effected. We concluded from this that the conversion of **2** to **3** is probably a photochemical process which

Table 2

Molecular Dimensions

(a) Bond Lengths (Å)

S(1) - C(2)	1.739(3)	C(17) - C(18)	1.362(5)
C(2) - N(3)	1.338(3)	C(18) - C(19)	1.379(5)
C(2) - S(6)	1.669(3)	C(19) - C(14)	1.371(4)
N(3) - N(4)	1.380(3)	C(16) - F(20)	1.368(3)
N(3) - C(13)	1.462(3)	N(9) - H(9)	0.835(21)
N(4) - C(5)	1.296(3)	C(10) - H(10A)	0.948(3)
C(5) - S(1)	1.741(2)	C(10) - H(10B)	0.953(3)
C(5) - N(7)	1.370(3)	C(10) - H(10C)	0.943(3)
N(7) - C(8)	1.400(3)	C(12) - H(12A)	0.946(3)
N(7) - C(12)	1.469(3)	C(12) - H(12B)	0.953(3)
C(8) - N(9)	1.331(3)	C(12) - H(12C)	0.945(3)
C(8) - O(11)	1.216(3)	C(13) - H(13A)	0.953(3)
N(9) - C(10)	1.452(3)	C(13) - H(13B)	0.960(3)
C(13) - C(14)	1.501(4)	C(15) - H(15)	0.952(3)
C(14) - C(15)	1.369(3)	C(17) - H(17)	0.956(3)
C(15) - C(16)	1.363(4)	C(18) - H(18)	0.956(3)
C(16) - C(17)	1.335(4)	C(19) - H(19)	0.942(3)

(b) Selected Dihedral Angles (°)

S(1)-C(5)-N(7)-C(8)	3.171	N(4)-C(5)-N(7)-C(12)	2.364
C(2)-N(3)-C(13)-C(14)	102.258	C(5)-S(1)-C(2)-S(6)	178.292
N(3)-N(4)-C(5)-N(7)	179.426	C(5)-N(7)-C(8)-N(9)	179.100
N(3)-C(13)-C(14)-C(15)	-73.868	C(5)-N(7)-C(8)-O(11)	-2.002
N(3)-C(13)-C(14)-C(19)	106.341	N(7)-C(8)-N(9)-C(10)	-176.814

(c) Bond Angles (°)

C(2)-S(1)-C(5)	89.362	N(7)-C(8)-N(9)	116.318
S(1)-C(2)-N(3)	107.948	N(7)-C(8)-O(11)	120.259
S(1)-C(2)-S(6)	124.947	N(9)-C(8)-O(11)	123.413
N(3)-C(2)-S(6)	127.083	C(8)-N(9)-C(10)	120.928
C(2)-N(3)-N(4)	118.521	N(3)-C(13)-C(14)	111.483
C(2)-N(3)-C(13)	125.880	C(13)-C(14)-C(15)	119.514
N(4)-N(3)-C(13)	115.536	C(13)-C(14)-C(19)	121.762
N(3)-N(4)-C(5)	109.262	C(15)-C(14)-C(19)	118.723
S(1)-C(5)-N(4)	114.905	C(14)-C(15)-C(16)	118.868
S(1)-C(5)-N(7)	124.481	C(15)-C(16)-C(17)	123.525
N(4)-C(5)-N(7)	120.614	C(15)-C(16)-F(20)	118.623
C(5)-N(7)-C(8)	119.054	C(17)-C(16)-F(20)	117.827
C(5)-N(7)-C(12)	117.724	C(16)-C(17)-C(18)	118.018
C(8)-N(7)-C(12)	123.215	C(17)-C(18)-C(19)	120.348
		C(14)-C(19)-C(18)	120.514

may proceed *via* the formation of sulphine and oxathiirane [9] or dioxathietane [10] intermediates.

In view of the large number of 2-alkyl(aryl)thio-1,3,4-thiadiazol-5-ylureas which have been described as herbicides [11], and the apparently facile nature of the rearrangements we have described, we believe it is now necessary to question the identity of the true active component in these studies [11]. This becomes especially important in view of the herbicidal activity described by Sasse and Eue [12] for various 3-substituted-1,3,4-thiadiazolin-2-one-(thione)-5-ylureas.

EXPERIMENTAL

All chemicals were of the highest purity available and were used as received, unless otherwise noted. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Pmr spectra were recorded on a Varian EM-390 spectrometer. The ^{13}C-nmr spectra were recorded on a Varian XL-200 spectrometer. All nmr peak positions are reported relative to tetramethylsilane. Mass spectra were recorded on a Varian MAT-CH7 spectrometer which was interfaced to an SS-200 data system. Infrared spectra were recorded on a Perkin-Elmer 297 spectrophotometer. Elemental analyses were performed on a Perkin-Elmer Model 240 elemental analyzer with IBM 1134 processing.

Preparative liquid chromatography was carried out on a Waters Prep LC/System 500A equipped with dual silica cartridges. Analytical hplc was carried out on an Altex Model 100 chromatograph equipped with an 8 μl uv detector, C-R1A recording data processor, and an IBM reverse-phase analytical column (C-18, 4.5 × 250 mm, 5 μ particle). The following solvent systems were used in the course of this study: A, 30% ethyl acetate/methylene chloride; B, 10% ethyl acetate/methylene chloride; C, 50% methanol/water; D, 70% methanol/water.

2-Mercapto-5-methylamino-1,3,4-thiadiazole (**4a**).

To a solution of 4-methyl-thiosemicarbazide (10.52 g, 0.1 mole) in anhydrous dimethylformamide (50 ml) was added carbon disulfide (19.0 g, 0.25 mole) dropwise over a two hour period. Following the addition, the mixture was stirred for one hour at room temperature, heated to 90° for four hours, then cooled to room temperature. The mixture was then poured into water (600 ml), chilled in an ice bath, and the precipitate collected. After washing with heptane (2 × 250 ml), the product was dried *in vacuo* at 50° overnight. Yield: 10.60 g (72%). Extraction of the aqueous filtrate with chloroform followed by drying (magnesium sulfate) and removal of solvent afforded an additional 2.43 g of the desired product, mp 190-193° (lit 188-194° [13]); ms: 147 (M+), 76 (CS_2), 71 (M - CS_2), 59, 42, 28. The product was carried on without further purification.

2-[^{13}C]-2-Mercapto-5-methylamino-1,3,4-thiadiazole (**4b**).

The labeled compound was prepared by essentially the same procedure described above, with the following modifications. [^{13}C]-Carbon disulfide (0.50 g, 6.57 mmoles, 90 atom %, Merck) was added in two equal portions at 20 minute intervals, followed by unlabeled carbon disulfide (0.50 g, 6.57 mmoles), again in two portions at 20 minute intervals. The mixture was then stirred for the requisite time and heated appropriately. Following normal workup, **4b** was isolated in 66% yield. The relative intensities of m/z 148 *vs.* 147 suggested a 52.7% enrichment.

2-(3-Fluorobenzylthio)-5-methylamino-1,3,4-thiadiazole (**5a**).

A suspension of 2-mercapto-5-methylamino-1,3,4-thiadiazole (7.375 g, 50 mmoles) was prepared in 2 *M* potassium hydroxide (25 ml), stirred for 10 minutes at room temperature, then treated with 3-fluorobenzyl chloride (7.25 g, 50 mmoles), added in one portion. The reaction was immediately diluted with methanol (50 ml), the reaction becoming slightly exothermic and kept below 35° with an ice bath. The mixture was stirred for 30 minutes at room temperature, during which time the product precipitates. This was collected, washed with heptane (250 ml), and dried *in vacuo* to afford 11.75 g (92%) of analytically pure material. mp 77-79°; pmr (deuteriochloroform): δ 7.3-6.8 (m, 5H, Ar and NH), 4.20 (s, 2H, CH_2-S), 2.93 (s, 3H, CH_3); ir (potassium bromide): 3200 (NH), 3000 (CH), 1620, 1580, 1560, 1410, 1260, 1240, 1055, 950, 910, 795, 715 cm^{-1} (1,3-disubstituted aromatic); ms: 255 (M$^+$), 222 (M - SH), 166, 129, 109 (C_7H_6F), 83 (C_5H_4F), 74, 57, 45, 28.

Anal. Calcd. for $C_{10}H_{10}FN_3S_2$: C, 47.04; H, 3.95; N, 16.46. Found: C, 46.9; H, 3.8; N, 16.7.

2-[^{13}C]-2-(3-Fluorobenzylthio)-5-methylamino-1,3,4-thiadiazole (**5b**).

Utilizing the procedure described for **5a** above, the desired product was isolated in 94% yield at the 4.0 mmole scale; ms: 256 (M+), 255 (M - 1), 223 (M - SH), 222, 167, 166, 109, 83, 74, 57, 45, 28. The relative intensities of m/z 256 *vs.* 255 and 223 *vs.* 222 suggest a 51.8% enrichment.

Anal. Calcd. for $C_{10}H_{10}FN_3S_2$: C, 47.04; H, 3.95; N, 16.46. Found: C, 47.0; H, 3.9; N, 16.4.

1,3-Dimethyl-1-(2-(3-fluorobenzylthio)-1,3,4-thiadiazol-5-yl)urea (**1a**).

To a solution of **5a** (8.93 g, 35.0 mmoles) in dry methylene chloride (250 ml) was added a catalytic amount of DABCO (350 mg) followed by the dropwise addition of methyl isocyanate (4.00 g, 70.0 mmoles). The mixture was stirred at room temperature under nitrogen for two hours, heated to reflux for two hours, cooled to room temperature, and evaporated to dryness. The residue was recystallized twice from ethyl acetate/hexane to afford the desired product in 81% yield. mp 115-116°; pmr (deuteriochloroform/dimethylsulfoxide-d_6): δ 7.4-6.7 (m, 5H, Ar and NH), 4.37 (s, 2H, CH_2-Ar), 3.57 (s, 3H, CH_3-N), 2.87 (d, 3H, CH_3-N, J = 4.4 Hz); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 163.4 (s, C-5 thiadiazole), 162.8 (d, C-3′ aromatic), 159.0 (s, C-2 thiadiazole), 155.2 (s, C=O), 139.1 (d, C-1′ aromatic), 130.2 (dd, C-5′ aromatic), 124.7 (d, C-6′ aromatic), 115.9 (dd, C-2′ aromatic), 114.6 (dd, C-4′ aromatic), 38.0 (t, CH_2-Ar), 33.8 (q, CH_3-N), 27.7 (q, CH_3-N); the distinction between 115.9 and 114.6 is made solely on the basis of the benzylic methylene next to 115.9 and could be reversed; ir (potassium bromide): 3400 (NH), 3060 and 2950 (CH), 1667 (C=O), 1547, 1480, 1410, 1325, 1215, 1105, 950, 798 cm^{-1}; ms: 312 (M$^+$), 255 (M - CH_3NCO), 222 (255 - SH), 166 (222 - CH_3NHCN), 109 (C_7H_6F), 74, 58, 28.

Anal. Calcd. for $C_{12}H_{13}FN_4OS_2$: C, 46.14; H, 4.19; N, 17.93. Found: C, 46.1; H, 4.2; N, 17.8.

1,3-Dimethyl-1-(2-(3-fluorobenzylthio)-2-[^{13}C]-1,3,4-thiadiazol-5-yl)urea (**1b**).

The compound was prepared as described for **1a**, yield, 874 mg (80%), mp 115-116°; ms: 313 (M$^+$), 312, 256 (M - CH_3NCO), 255, 223 (256 - SH), 222, 167, 166, 109, 83, 74, 58, 28. The relative intensities of m/z 313 *vs.* 312 and 223 *vs.* 222 suggest a 51.6% enrichment.

Anal. Calcd. for $C_{12}H_{13}FN_4OS_2$: C, 46.14; H, 4.19; N, 17.93. Found: C, 46.1; H, 4.1; N, 18.3.

Isolation of Photoproducts.

A solution of **1** (1.500 g) in acetone (100 ml) was evenly distributed on the inner surface of glass dishes, forming a thin film at a rate of 15 μg/cm^2. After the acetone had evaporated, the dishes were exposed to a mixture of artificial and natural light (16 hour light, 8 hour dark cycle) in a glass house for four days (June 3-6, 1983). The dishes were then rinsed with methylene choride to remove **1** and its photoproducts.

The photolysis mixture was fractionated by preparative layer chromatography (Whatman PLK5F, 20 × 20 cm, 1000 μ, 50 mg/plate), eluting with system B. Two uv-active bands were detected. The less polar band (Rf = 0.39) was extracted with acetone, evaporated to dryness, and recrystallized from absolute ethanol, affording 213 mg of **2**. The second band (Rf = 0.18) was similarly extracted, affording a mixture of **1** and **3**, as detected by reverse-phase analytical hplc (system C). The two components were separated by reverse-phase preparative layer chromatography (Whatman PKC$_{18}$, 20 × 20 cm, 1000 μ), developing each plate twice to enhance the separation (system D). Two uv-active bands were detected

(Rf = 0.38 and 0.27), isolated, extracted with acetone, and recrystallized from ethanol, affording **3** (176 mg) and **1**, respectively.

Photoproduct (**2**).

This compound had mp 178-179°; pmr (1:1 dimethylsulfoxide-d_6:acetone-d_6): δ 7.52 (q, 1H, NH, J = 6.0 Hz), 7.40-6.97 (m, 4H, Ar), 5.42 (s, 2H, CH_2-Ar), 3.30 (s, 3H, CH_3-N), 2.68 (d, 3H, CH_3-N, J = 6.0 Hz); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 183.1 (s, C-2 thiadiazole), 162.1 (d, C-3′ aromatic), 155.0 (s, C=O), 153.2 (s, C-5 thiadiazole), 137.2 (d, C-1′ aromatic), 127.1 (dd, C-5′ aromatic), 120.2 (d, C-6′ aromatic), 118.0 (dd, C-2′ aromatic), 110.9 (dd, C-4′ aromatic), 52.1 (t, CH_2-Ar), 32.5 (q, CH_3-N), 27.8 (q, CH_3-N); the assignments of C-2′ and C-4′ are based on C-2′ being adjacent to the methylene and could be reversed; ir (potassium bromide): 3340 (NH), 2950 (CH), 1675 (C=O), 1597 (1,3-disubstituted aromatic), 1515, 1405 (C=S), 1345, 1185 (C=S), 1058, 958, 870, 795 (1,3-disubstituted aromatic), 750, and 712 cm^{-1} (1,3-disubstituted aromatic); ms: 312 (M^+), 255 (M - CH_3NCO), 222 (255 - SH), 166, 109 (C_7H_6F), 83 (C_5H_4F), 74 (CH_3NHCS), 57 (CH_3NCO).

Anal. Calcd. for $C_{12}H_{13}FN_4OS_2$: C, 46.14; H, 4.19; N, 17.93. Found: C, 46.1; H, 4.2; N, 17.9.

Photoproduct (**3**).

This compound had mp 183-185°; pmr (1:1 dimethylsulfoxide-d_6:acetone-d_6): δ 7.45-6.85 (m, 5H, NH and Ar, one proton exchanges with deuterium oxide), 4.95 (s, 2H, CH_2-Ar), 3.27 (s, 3H, CH_3-N), 2.73 (d, 3H, CH_3-N, J = 5.2 Hz); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 168.4 (s, C-2 thiadiazole), 166.5 (s, C-5 thiadiazole), 162.7 (d, C-3′ aromatic), 155.3 (s, C=O), 139.2 (s, C-1′ aromatic), 127.0 (dd, C-5′ aromatic), 120.0 (d, C-6′ aromatic), 118.0 (dd, C-2′ aromatic), 110.8 (dd, C-4′ aromatic), 48.4 (t, CH_2-Ar), 34.3 (q, CH_3-N), 28.5 (q, CH_3-N); ir (potassium bromide): 3356 (NH), 2940 (CH), 1672 (C=O), 1647 (C=O), 1598 (1,3-disubstituted aromatic), 1528, 1378, 1333, 1253, 1220, 962, 780 (1,3-disubstituted aromatic), 756, 745, 708 cm^{-1} (1,3-disubstituted aromatic); ms: 296 (M^+), 239 (M - CH_3NCO), 197, 150, 124, 109 (C_7H_6F), 83 (C_5H_4F), 74 (CH_3NHCS), 58, 57, 28.

Anal. Calcd. for $C_{12}H_{13}FN_4O_2S$: C, 48.64; H, 4.42; N, 18.91. Found: C, 48.9; H, 4.5; N, 18.5.

Solution Photolysis of **1**.

A solution of **1** (3.50 g, 11.2 mmoles) in methylene choride (350 ml) was photolyzed under nitrogen for four hours with cooling to 32°, using a 450 Watt Hanovia mercury arc lamp. After evaporation of the solvent, the residue was chromatographed on a Waters System 500A Prep LC (system A). The two uv-active materials were collected separately, evaporated to dryness, and characterized. The first material eluted (1.41 g, 40%) was found to be identical with **2** isolated from the thin film photolysis. The second material eluted (1.62 g, 46%) was identified as recovered **1** on the basis of tlc mobility (Whatman LHP-KF, system B) and pmr spectra.

Kinetics of Photolysis of **1**.

A solution of **1** (3.50 g) in methylene chloride (350 ml) was photolyzed as described previously. At various time points, aliquots were withdrawn, a 5.0 ml sample evaporated to dryness *in vacuo*, dissolved in deuteriochloroform (0.75 ml) and analyzed by pmr. The absorptions at δ 5.42 and δ 4.37 were integrated and the relative intensities taken as an indication of the concentrations of **2** and **1**, respectively.

In a similar manner, a 0.5 ml aliquot of each photolysis sample was evaporated to dryness, dissolved in 2.00 ml of acetonitrile, and analyzed by reverse-phase hplc (system C, 1.0 ml/minute). Although a number of minor components (<1.0%) could be detected toward the end of the photolysis (6 hours), only two major components were detected. The relative concentrations of **1** (retention time = 7.4 minutes) and **2** (retention time = 10.3 minutes) were determined from the area under the respective peaks.

N-Methyl-2-(3-fluorophenylmethylene)hydrazinecarbothioamide (**6**).

To a solution of 4-methylthiosemicarbazide (10.52 g, 0.1 mole) in boiling ethanol (150 ml) on a steam bath was added 3-fluorobenzaldehyde (12.41 g, 0.1 mole). The mixture was heated an additional 20 minutes, rapidly chilled in an ice bath, and the crystals which formed were collected. Recrystallization from ethanol afforded the desired product in 84 to 86% yield. mp 177-179°; pmr (dimethylsulfoxide-d_6): δ 11.48 (br s, 1H, NH), 8.56 (q, 1H, NH, J = 4.2 Hz), 8.03 (s, 1H, CH=N), 7.78 (dd, 1H, H-2, $J_{H,F}$ = 9.9 Hz, $J_{2,6}$ = 2.7 Hz), 7.6-7.0 (m, 3H, Ar), 3.06 (d, 3H, CH_3-N, J = 4.2 Hz); ir (potassium bromide): 3380 (NH), 3160 and 3000 (CH), 1550 and 1270 (C=S), 1530 (C=N), 753 and 682 cm^{-1} (1,3-disubstituted aromatic); ms: 211 (M^+), 180 (M - CH_3NH_2), 137 (180 - C=S), 122 (137 - NH), 95 (C_6H_4F), 90 ($NH_2CSNHCH_3$), 74 (90 - NH_2), 57 (90 - SH).

Anal. Calcd. for $C_9H_{10}FN_3S$: C, 51.17; H, 4.77; N, 19.89. Found: C, 51.1; H, 4.8; N, 20.0.

1-(3-Fluorobenzyl)-4-methylthiosemicarbazide (**7**).

Following the general procedure of Sasse [8], a solution of **6**, (16.90 g, 80.0 mmoles) in ethylene glycol monomethyl ether (100 ml) was treated with sodium borohydride (1.61 g, 43.0 mmoles) in small portions to avoid excessive foaming. Additional sodium borohydride (1.61 g, 43.0 mmoles) was dissolved in water (20 ml) and added to the mixture dropwise while gently warming the solution. Following the addition, the reaction was heated to reflux for two hours, cooled to room temperature, evaporated to a heavy oil and acidified (*p*H 5.0) with 20% hydrochloric acid. After refrigerating overnight, the product was collected by filtration, yield, 79%, mp 121-124°; pmr (dimethylsulfoxide-d_6): δ 11.60 (br s, 1H, NH), 8.58 (q, 1H, NH, J = 4.6 Hz), 7.80 (br t, 1H, NH), 7.6-6.9 (m, 4H, Ar), 3.06 (d, 2H, CH_2-N), 2.87 (d, 3H, CH_3-N); ms: 213 (M^+), 211 (M - 2H), 180 (211 -CH_3NH_2), 137 (180 - C=S), 124 (C_7H_6FNH+), 109 (C_7H_6F), 95 (C_6H_4F), 90 ($NH_2CSNHCH_3$), 74 (CH_3NHCS), 57 (90 - SH), 30 (CH_3NH).

1,3-Dimethyl-1-(3-(3-fluorobenzyl)-1,3,4-thiadiazolin-2-one-5-yl)urea (**3**).

To a solution of **7** (2.133 g, 10.0 mmoles) in dry chloroform (12.5 ml) was added a solution of phosgene in toluene (12.5% w/w, 1.98 g, 20.0 mmoles) keeping the temperature between 10° and 20°. Following the addition, a weak stream of phosgene gas was introduced into the mixture while heating to reflux for three hours. After cooling to room temperature, the mixture was evaporated to dryness, the residue dissolved in dry acetone (12.5 ml), chilled to 5°, and diethyl ether saturated with methylamine added until the formation of methylamine hydrochloride above the mixture ceased. The mixture was stirred another 10 minutes, water added (50 ml), the precipitate which formed collected, and the filtrate extracted with methylene chloride (3 × 75 ml). After removing the solvent *in vacuo*, the residue was recrystallized twice from ethanol, affording the desired photoproduct **3**. Recrystallization of the first precipitate collected provided additional **3** total yield, 1.02 g (35%). The ir, pmr, ^{13}C-nmr, and mass spectra, melting point, mixed melting point, and hplc chromatographic behaviour (C-18 reverse-phase, system C) were identical with that previously described for **3**.

Attempted Preparation of Photoproduct **3** by Hydrolysis of Photoproduct **2**.

A solution of **2** (0.500 g, 1.605 mmoles) in ethanol (15 ml) was treated with 40 ml of distilled water, 1.0 *N* hydrochloric acid, or 2.0 *N* sodium hydroxide for 48 hours at reflux. A similar solution was also treated with 40 ml of 2.0 *N* sodium hydroxide for 48 hours at room temperature. After cooling the solutions to room temperature, the mixtures were extracted with chloroform (3 × 50 ml), dried (magnesium sulfate), filtered, and evaporated to dryness. With water, 1.0 *N* hydrochloric acid, and 2.0 *N* sodium hydroxide at room temperature, **2** was recovered unchanged in 94 to 96% yield. In the case of the refluxing base treatment, a light colored oil was isolated (0.403 g); pmr (deuteriochloroform): δ 7.4-6.75 (m, 4H, Ar), 5.73 (q, 1H, NH, J = 4.5 Hz), 5.26 (s, 2H, CH_2-Ar), 2.81 (d, 3H, CH_3-N); ms: 255 (M^+), 222 (M - SH), 199 (M - CH_3NHCN), 166 ($C_6H_4FCHNCS$), 124, 109, 83, 74, 57.

X-Ray Analysis of Photoproduct **2**.

The crystal used had approximate dimensions 0.17 × 0.50 × 0.26 mm. After preliminary examination, unit cell dimensions and density

data were measured on an ENRAF-NONIUS CAD4 diffractometer with monochromated Mo-Kα radiation using Ψ-scans. Of 2313 observed reflections, 1409 with intensity, I, greater than $2\sigma(I)$ were used in solving the structure.

The structure was solved by direct methods. The positions of the two sulfur atoms were found from a Patterson map. The remaining atoms were located from successive Fourier maps. All of the hydrogens could be seen in a difference Fourier map after the heavy atoms had been refined, except the C-10 hydrogens. The N-9 hydrogen was refined since there was no idealized position suitable for use. All remaining hydrogen atoms were placed at idealized positions. Two sets of half-hydrogens, staggered and eclipsed with respect to the C-10 -- N-9 bond were used on C-10. The refinement converged to R = 0.036.

Crystal Data (**2**).

Monoclinic, a = 13.057(2), b = 8.449(2), c = 13.703(2) Å, β = 102.23(2)°, Z = 4, Dc = 1.404.

Systematic extincitons: OkO, k odd; hO1, h + 1 odd; space group $P2_1/n$.

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