Reaction of Oxaziridine with Sulfur-Containing Heterocumulenes

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The reactions of oxaziridines **1** with carbon disulfide (**2**) and phenyl isothiocyanate (**8**) have been studied. With carbon disulfide, 2-*n*-alkyl- or *sec*-alkyloxaziridines give alkyl isothiocyanates (quantitatively), carbonyl compounds, and sulfur. Similar reactions between **1** and **8** form carbodiimides **9**, but under mild experimental conditions **1** and **8** react to yield considerable amounts of either and/or the thiadiazolidinethione isomers **10** and **11**. 2-*tert*-Butyloxaziridine **1f** does not react with **2**, but reacts with **8** to afford oxadiazolidinethione **12** and oxadiazolidinone **13**.

In the preceding paper,[1] we reported the reactions of oxaziridines with a ketene, isocyanates, and a carbodiimide, showing that the results are quite different from those of oxiranes and of aziridines. In the reactions, oxaziridines gave 1:1 cycloadducts or unstable three-membered intermediates, which further reacted with the cumulenes to give stable heterocycles, with the release of carbonyl compounds.

In the present study, the reactions with sulfur-containing heterocumulenes such as carbon disulfide and an isothiocyanate are described. From one heterocumulene, in these reactions, another heterocumulene was obtained along with a carbonyl compound and sulfur *via* unstable intermediates. The further reactions of the intermediates giving heterocycles were also observed.

Such a characteristic difference caused by a sulfur atom, which is generally a good leaving group or easily exchangeable with an oxygen atom, can be expected from the following reactions of the cumulenes. In the reactions with ethylene oxide, for example, carbon disulfide gives ethylene carbonate and ethylene trithiocarbonate[2,3] and phenyl isothiocyanate gives 1,3-oxazolidin-2-one[4,5] or isocyanate trimer,[4,6] though 1:1 cycloadditions are observed in the reactions of propylene oxide,[3] ethylene sulfide,[3] or aziridines[7,8] with carbon disulfide, aziridines with phenyl isothiocyanate,[8] and ethylene oxide with *N*-acyl isothiocyanate.[5]

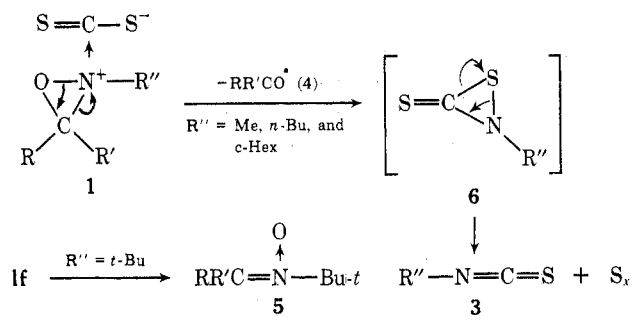
Results and Discussion

Reaction with Carbon Disulfide. In the reaction of 2-*n*-alkyl- or 2-cycloalkyloxaziridine **1a,c,e,g,j** with carbon disulfide (**2**), an isothiocyanate **3** was quantitatively obtained. The results are shown in Table I.

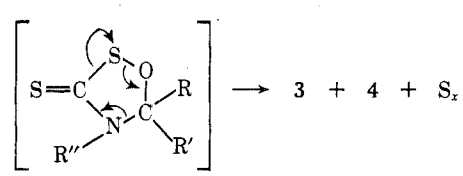
The products were characterized by the strong infrared absorption band at 2120 cm^{-1} (N=C=S). They were identified and determined by glpc or by converting them into thiourea derivatives. No reaction was observed for 2-*tert*-butyloxaziridine **1f** in refluxing carbon disulfide; and the rearrangement of the oxaziridine **1f** to α-phenyl-*N*-*tert*-butylnitrone (**5**) occurred under severe conditions, but a small quantity of *tert*-butyl isothiocyanate was detected by ir and glpc.

The reaction is assumed to proceed *via* a thiaziridinethione intermediate **6** (Scheme I), which readily decomposes into an isothiocyanate **3** and sulfur. A similar assumption has been proposed for the reactions of the oxaziridines with diphenylketene and with diphenylcarbodiimide. The decomposition of the intermediate **6** occurs much faster than its further reaction with carbon disulfide because of the poor stability of the intermediate **6** caused by the sulfur atom in the ring and because of the low electrophilicity of carbon disulfide. In this reaction, an unstable thioperoxy intermediate **7**, a 1:1 cycloadduct of an oxaziridine and carbon disulfide, is also possible, taking into

Scheme I



account the strong affinity of sulfur and oxygen along with a large ring strain of the intermediate **6**. Such intermediates having a sulfur–oxygen bond are known in many reactions, for example, synthesis of sulfinylimine from *p*-toluenesulfonamide and a sulfoxide *via* a 1,3-dioxa-2,4,6,5-trithiazine intermediate.[9]



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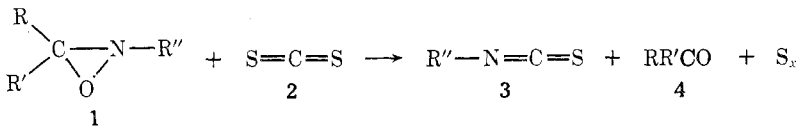
The reason for no reaction of the oxaziridine **1f** with carbon disulfide other than the rearrangement of **1f** to an isomeric nitrone is apparently due to a combination of factors involving both the steric hindrance to addition by the bulky *N*-*tert*-butyl moiety and the low electrophilicity of carbon disulfide.

Reaction with Phenyl Isothiocyanate. It is very interesting to observe whether an isothiocyanate will behave like carbon disulfide or an isocyanate in the reaction with oxaziridines. A carbodiimide should be given in the former case and a 1:1 cycloadduct in the latter.

At 110°, the reaction of 2-cyclohexyl-3-phenyloxaziridine (**1e**) gave *N*-cyclohexyl-*N*′-phenylcarbodiimide (**9e**) with benzaldehyde and sulfur, showing that the reaction surely proceeded by such a mechanism as assumed in the reaction with carbon disulfide. Though carbonyl compounds and sulfur were quantitatively obtained in the reactions of other 2-*n*-alkyl- or *sec*-alkyloxaziridines **1a–d,k**, none of the corresponding carbodiimides were isolated. This was because of polymerization of the resulting carbodiimides.

The reaction was remarkably changed with a decrease in the reaction temperature. At 90°, the reaction of these oxaziridines gave thiadiazolidinethione derivatives **10**, **11**, and benzaldehyde. That not only a considerable amount of sulfur was isolated but also benzaldehyde was obtained in more than 100% yield (calculated based on the reaction

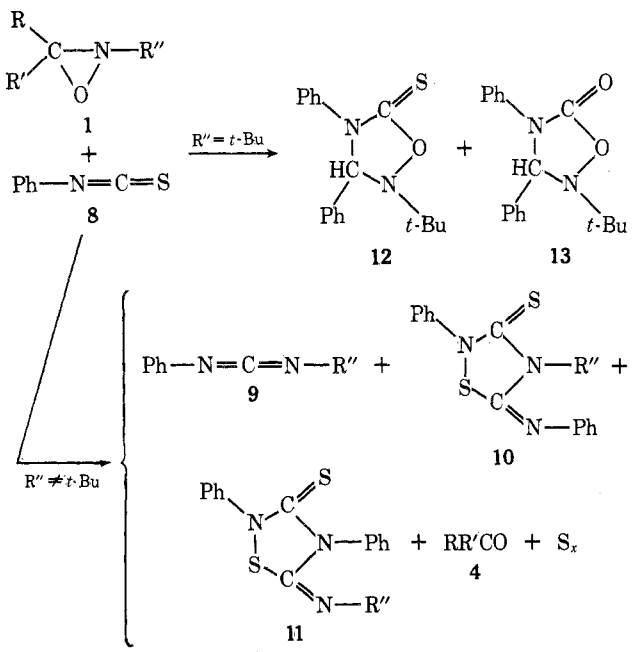
Table I
Reaction of Oxaziridine with Carbon Disulfide



Oxaziridine (1)				Reaction[a] time, hr	Yield, %[d]			
	R	R′	R″		3	4	S_x	RR′C=N—R″ (O)
1a	C_6H_5	H	CH_3	6.0	97	100	92	
1c	C_6H_5	H	n-C_4H_9	7.0	55[e]	61[e]	84	
1e	C_6H_5	H	c-C_6H_{11}	7.5	84	90	82	
1g	C_6H_5	CH_3	n-C_4H_9	5.0	84	98	100	
1j	$-(CH_2)_5-$		CH_3	5.0	94	100	93	
1f	C_6H_5	H	t-C_4H_9	30.0				*f*
1f	C_6H_5	H	t-C_4H_9	33.0[b]				38[g]
1f	C_6H_5	H	t-C_4H_9	7.0[c]	*h*	*h*		95

[a] Refluxed with excessive amount of **2**. [b] At 70° in a sealed tube. [c] At 100° in a sealed tube. [d] Yields of **3** and **4** were determined by glpc. [e] Determined by distillation. [f] Unreacted **1f** was recovered quantitatively. [g] Unreacted **1f** was recovered. [h] t-BuNCS, PhCHO, and t-BuN=CHPh were detected by ir and glpc but not isolated.

between 1 mol of **1** and 2 mol of **8**) indicates that the reactions include the path leading to a carbodiimide **9**.



2-*tert*-Butyloxaziridine **1f**, on the other hand, gave the 1:1 cycloadduct, oxadiazolidinethione **12**, in a good yield with a small amount of oxadiazolidinone **13**.

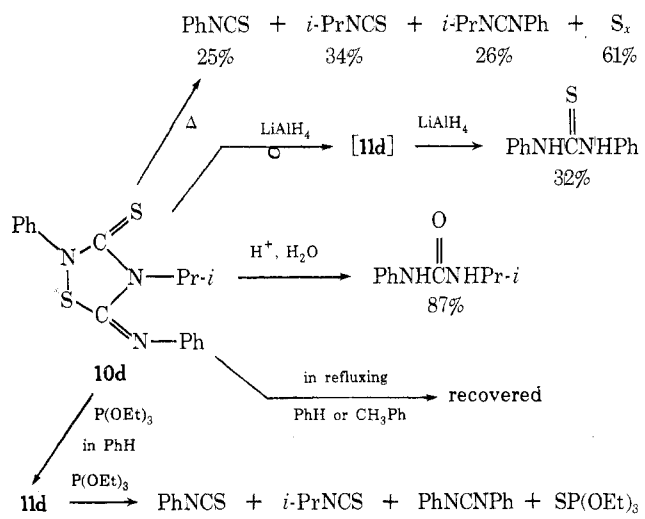
No reaction was observed between the isothiocyanate and 2-benzoyloxaziridine **1i**, which rearranged to 2,2-pentamethylene-5-phenyl-1,3,4-dioxazoline.[10]

The results are given in Table II.

The carbodiimide **9e** showed a strong infrared absorption band at *ca.* 2150 cm^{-1} and was confirmed as *N*-cyclohexyl-*N*′-phenylurea by hydration.

The structures of the two thiadiazolidine isomers **10** and **11** were determined by the spectral and analytical data and pyrolysis. The infrared absorption of the C=N stretching vibration of **10** appears at 1610–1615 cm^{-1}, *ca.* 20 cm^{-1} lower than that of **11**. In nmr spectra, the signals of the *N*-methylene or *N*-methine proton of **10** were observed in higher field than those of **11** by 0.7–2.0 ppm. Such a thidiazolidine ring system seems to be relatively stable and, for example, 2,4-diphenyl-3,5-bis(phenylimino)-1,2,4-thiadiazolidine is readily formed by acidic oxidation of *N*,*N*′-diphenylthiourea.[11]

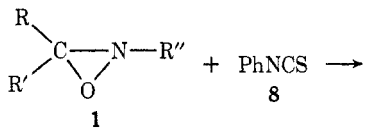
Pyrolysis of **10d** at 185° under a nitrogen stream gave isopropyl isothiocyanate, phenyl isothiocyanate, *N*-isopropyl-*N*′-phenylcarbodiimide, and sulfur. These products well supported the structure of **10d**. The compound **10d** was unchanged when it was heated in refluxing benzene or toluene, but rearranged to the isomer **11d** (61% yield) when a catalytic amount of triethyl phosphite was added to the solution. A large amount of the phosphite caused desulfurization to give phenyl isothiocyanate (17%), isopropyl isothiocyanate (17%), diphenylcarbodiimide (7%), the rearranged isomer **11d** (trace), and triethyl phosphite (64%). Reduction with $LiAlH_4$ and acidic hydrolysis of the compound **10d** gave *N*,*N*′-diphenylthiourea and *N*-isopropyl-*N*′-phenylurea, respectively. The former may be formed *via* the rearranged isomer **11d**.



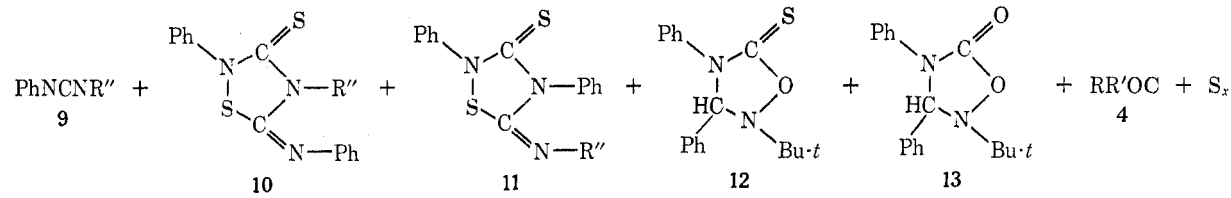
The strucure of the major product of the reaction of the oxaziridine **1f** with phenyl isothiocyanate, namely 2-*tert*-butyl-3,4-diphenyl-1,2,4-oxadiazolidine-5-thione (**12**), was also determined by spectral and analytical data. The minor product, 2-*tert*-butyl-3,4-diphenyl-1,2,4-oxadiazolidin-5-one (**13**), is identical with the cycloadduct of the oxaziridine and phenyl isocyanate.[1]

A possible reaction scheme to explain the products of the reaction of oxaziridines with phenyl isothiocyanate involves the formation of a thiaziridineimine intermediate **14** with the release of a carbonyl compound **4**. At higher temperatures the intermediate **14** thermally decomposes into a carbodiimide **9** and sulfur (Scheme II) as postulated for the reaction of oxaziridines with carbon disulfide. At

Table II
Reaction of Oxaziridine with Phenyl Isothiocyanate



1 + 8 →

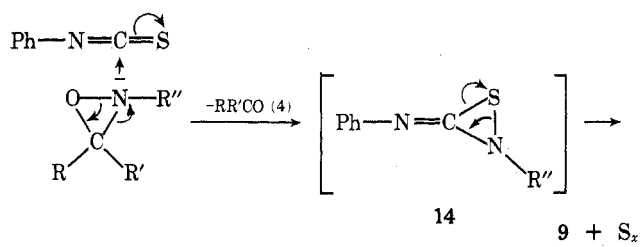


9 + 10 + 11 + 12 + 13 + 4 + S_x

Oxaziridine (1)				Conditions[a]			Yield, %						
	R	R′	R″	Mole ratio 1:8[b]	Temp, °C	Time,[c] hr	9[d]	10[e]	11[e]	12[d]	13[d]	4[e]	S_x[d]
1a	C_6H_5	H	CH_3	1.0	110	3.0						191	90
1e	C_6H_5	H	c-C_6H_{11}	1.0	110	3.0	58					192	82
1a	C_6H_5	H	CH_3	1.0	100	1.2		6				188	69
1b	C_6H_5	H	C_2H_5	0.6	85	2.6		22	4			119	19
1c	C_6H_5	H	n-C_4H_9	1.0	90	3.0		8	28			122	30
1d	C_6H_5	H	i-C_3H_7	0.7	90	5.5		36	1			98	1
1e	C_6H_5	H	c-C_6H_{11}	1.0	90	5.5		*g*	58			117	2
1f	C_6H_5	H	t-C_4H_9	1.0	105	2.0				68	19		
1i	$-(CH_2)_5-$		COC_6H_5	1.0	115[f]	7.0							*h*
1k	C_6H_5	H	$CH_2C_6H_5$	1.0	100	1.4		7				143	67

[a] Relatively small amount of benzene was added. [b] **8:** phenyl isothiocyanate. [c] Allowed to react until ir absorption of **8** disappeared. [d] Based on equimolar reactions. [e] Based on reaction between 1 mol of **1** and 2 mol of **8**. Hence, the yield of **4** is 200% when the reaction is completely equimolar. [f] Toluene was employed as a solvent. [g] The product corresponding to **10e** was detected by ir but could not be purified. [h] The oxaziridine **1i** rearranged to 2,2-pentamethylene-5-phenyl-1,3,4-dioxazoline in 53% yield.

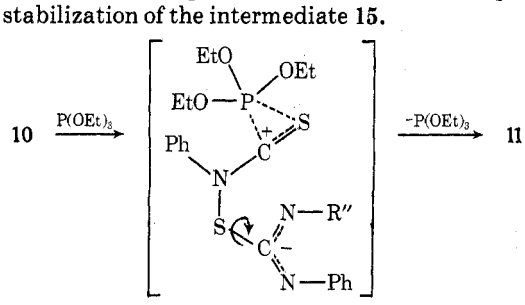
Scheme II



14

9 + S_x

lower temperatures, the intermediate **14** is somewhat more stable and it reacts with an additional molecule of the isothiocyanate, giving thiadiazolidinethiones. The formation of two isomers can be explained in terms of the two paths shown in Scheme III. The one is formed by the nucleophilic attack of the ring nitrogen atom to an isothiocyanate (path a) and the other is formed by the attack of the imino nitrogen atom (path b). According to the fact that the thiadiazolidine **10d** rearranged to the isomer **11d** in the presence of triethyl phosphite, possibility of the rearrangement of **10** to **11** during the reactions may not be excluded. The rearrangement is considered to be promoted by stabilization of the intermediate **15**.



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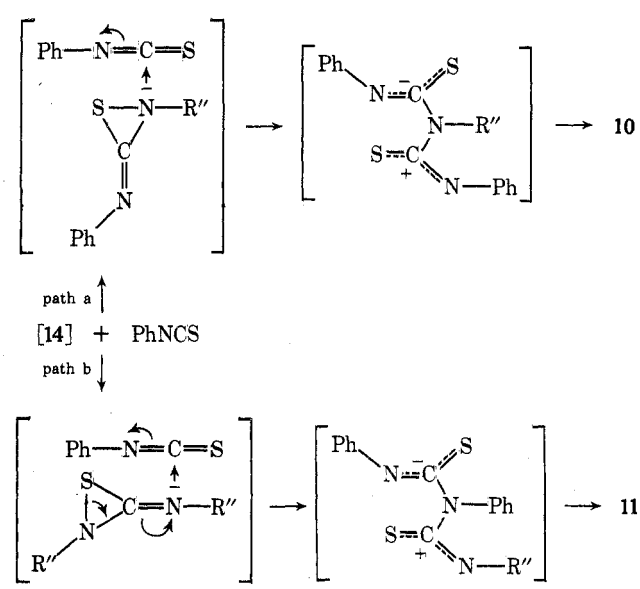
In the reaction giving thiadiazolidinethiones, the equimolar reaction forming a carbodiimide occurs simultaneously. Therefore, it is reasonable that a carbonyl compound was obtained in more than 100% yield when it is

Scheme III



calculated on the basis of the reaction giving thiadiazolidinethiones.

As an alternative mechanism, a 1:1 cycloadduct intermediate instead of the three-membered intermediate cannot be excluded for these reactions. This possibility is already mentioned in the reaction with carbon disulfide. Thermal decomposition and the further reaction of this intermediate will also lead to the reaction products.

The reaction of 2-*tert*-butyloxaziridine **1f** with phenyl isothiocyanate to yield the oxadiazolidinethione **12** can be rationalized by invoking the steric arguments used to explain the reaction of **1f** with isocyanates and a carbodiimide.[1] The formation of the minor product **13** is ascribed to the replacement of a sulfur atom by an oxygen atom of an oxaziridine during the reaction, as the ir spectrum of

the reaction mixture showed the formation of **13**, and partly to the replacement during column chromatography.

The difference from the reaction with carbon disulfide is due partly to the greater electrophilicity of the center carbon of an isothiocyanate, which is less than that of an isocyanate and comparable with that of a carbidiimide or a ketene, and partly to slightly larger stability of the intermediate **14** compared with the intermediate **6**.

Experimental Section

Melting points (uncorrected), ir, nmr, and mass spectra, and glpc data were obtained on the same apparatus reported in the preceding paper.[1] Mass spectrometry was performed at 70 eV. All the reactions were carried out under a nitrogen stream in the apparatus reported previously.[1]

Materials. Phenyl isothiocyanate was purchased from a commercial source.

2-Alkyloxaziridine **1a-g,k** and 2-benzoyloxaziridine **1i** were prepared by the procedures reported in the preceding paper[1] and the oxaziridine **1j** by Schmitz's method.[12] Boiling point and yields of 2-methyl-3,3-pentamethyleneoxaziridine (**1j**) and 2-benzyl-3-phenyloxaziridine (**1k**), which was used without distillation, are as follows: **1j**, bp 63-64° (13 mm), 50%; **1k**, 84%. The data on the other oxaziridines are described in the preceding paper.[1] The purities (active oxygen content: AO) were determined by iodometry.

A. Reaction with Carbon Disulfide. Reactions of the Oxaziridines 1a, 1g, and 1j. A mixture of the oxaziridine **1a** (8.1 g, 54 mmol, AO 90%) and carbon disulfide (**2**, 13.5 g, 178 mmol) was refluxed for 6 hr. After removal of the excess of **2**, 1.62 g (93%) of sulfur precipitated and was filtered off. The filtrate was distilled, but *N*-methyl isothiocyanate (**3a**) and benzaldehyde were not separated satisfactorily; infrared spectra of the distillates indicated absorption bands at about 2120 (N=C=S) and 1700 cm^{-1} (CHO). Determination of the yields and identification were made by glpc on the combined distillates.

The other two runs were carried out by the same procedure, starting with the oxaziridine **1g** (6.0 g, 28 mmol, AO 90%) and carbon disulfide (**2**, 10.0 g, 132 mmol), the oxaziridine **1j** (5.0 g, 34 mmol, AO 86%), and **2** (8.7 g, 114 mmol), respectively. The amount of sulfur precipitated was 0.91 (100%) and 1.0 g (93%), respectively.

Retention times of the products were identical with those of an authentic sample.[13] Operating conditions of glpc were as follows: column, 4 mm × 2 m Apiezon Grease L 10% on Diazolid L 60-80 mesh; carrier gas H_2, 34 ml/min; column temperature, 103 (CH_3NCS) and 145° (C_4H_9NCS); retention time, 1.6 min (CH_3NCS) and 3.7 min (C_4H_9NCS).

Reaction of Oxaziridine 1c and 1e. A mixture of the oxaziridine **1c** (10.2 g, 54 mmol, AO 94%) and carbon disulfide (**2**, 12.9 g, 170 mmol) was refluxed for 7 hr. After removal of the excess of **2** and of sulfur (1.45 g, 84%), the filtrate was treated with 40% $NaHSO_3$ and extracted (ether). The aqueous layer was treated with NaOH, extracted (ether), dried (Na_2SO_4), and distilled to give benzaldehyde (3.8 g, 66%). The ethereal solution was dried (Na_2SO_4) and distilled to afford *n*-butyl isothiocyanate (**3c**, 3.4 g, 55%), bp 76° (26 mm), ir (neat) 2120 cm^{-1} (-NCS). Furthermore, the compound **3c** was allowed to react with *n*-butylamine to give *N,N'*-di-*n*-butylthiourea: mp 64.5-65.5°; ir (Nujol) 3290 (NH), 1418 and 1215 (C=S), 1520 cm^{-1} (NH, CN).

Anal. Calcd for $C_9H_{20}N_2S$: C, 57.40; H, 10.70; N, 14.87. Found: C, 57.68; H, 10.79; N, 14.70.

The reaction of the oxaziridine **1e** (10.0 g, 44 mmol, AO 89%) with **2** (10.0 g, 132 mmol) was carried out as described above, and cyclohexyl isothiocyanate (**3e**, 5.2 g, 84%), benzaldehyde (4.2 g, 90%), and sulfur (1.15 g, 82%) were obtained. The isothiocyanate **3e** was treated with cyclohexylamine to give *N,N'*-dicyclohexylthiourea (**3e**), bp 85° (7.5 mm), ir (neat) 2120 cm^{-1} (-NCS), and thiourea, mp 185.5-187°, ir (Nujol) 3210 (NH), 1413 and 1226 (C=S), and 1505 cm^{-1} (NH, CN).

Anal. Calcd for $C_{13}H_{24}N_2S$: C, 64.95; H, 10.06; N, 11.65. Found: C, 64.94; H, 10.36; N, 11.79.

Reaction of the Oxaziridine 1f. A mixture of the oxaziridine **1f** (8.2 g, 45 mmol, AO 98%) and carbon disulfide (**2**, 11.0 g, 144 mmol) was refluxed for 30 hr. The oxaziridine was recovered quantitatively by distillation.

In a 25-ml glass tube, a mixture of the oxaziridine **1f** (8.0 g, 44 mmol, AO 98%) and **2** (5.4 g, 71 mmol) was sealed and allowed to stand at 70° for 33 hr. The excess of **2** was removed and the resultant solid was filtered and recrystallized (hexane) to give α-phenyl-*N*-*tert*-butylnitrone (3.0 g, 38%): mp 74-75° (mixture melting point of the mixture of the product and an authentic sample[14] was not depressed); ir (Nujol) 1562 (C=N), 1192, and 1120 cm^{-1} (NO); the spectrum was identical with that of the authentic sample.

Under severe conditions (100°, 7 hr), 6.8 g (95%) of the nitrone was obtained from the oxaziridine **1f** (8.1 g, 40 mmol, AO 88%) and the sulfide **2** (6.1 g, 80 mmol).

B. Reaction with Isothiocyanate. Reaction of the Oxaziridine 1a. To a solution of phenyl isothiocyanate (**8**, 10.0 g, 74 mmol) in benzene (10 ml), the oxaziridine **1a** (10.0 g, 52 mmol, AO 70%) was added dropwise with stirring and allowed to react for 2 hr. The temperature of the mixture was maintained at 110°. The mixture was distilled to give 7.5 g (191%) of benzaldehyde and a small amount of unreacted **8**. The residue was chromatographed (basic aluminum oxide-benzene) to give 1.5 g (90%) of sulfur.

At 100°, 3.6 g (188%) of benzaldehyde, 0.8 g (69%) of sulfur, and 0.30 g (6%) of 4-methyl-2-phenyl-5-phenylimino-1,2,4-thiadiazolidine-3-thione (**10a**) were obtained from the reaction between the oxaziridine **1a** (6.1 g, 37 mmol, AO 81%) and the isothiocyanate **8** (4.9 g, 36 mmol) for 1.2 hr.

Thiadiazolidinethione **10a** was obtained as pale yellow needles (from EtOH): mp 131-132.5°; ir (Nujol) 1610 cm^{-1} (C=N); mass spectrum *m/e* 299 (M^+, calcd 299), 226 ($M^+ - CH_3NCS$), 194 ($PhNCNPh^+$), 164 ($M^+ - PhNCS$), 132 ($PhNCNCH_3^+$), 135 ($PhNCS^+$).

Anal. Calcd for $C_{15}H_{13}N_3S_2$: C, 60.17; H, 4.37; N, 14.03. Found: C, 59.85; H, 4.10; N, 13.73.

Reaction of the Oxaziridine 1e. The reaction of the oxaziridine **1e** (11.0 g, 49 mmol, AO 91%) with the isothiocyanate **8** (7.7 g, 57 mmol) in 7 ml of benzene was carried out by the same procedure as above for 3 hr. The reaction mixture was distilled to give benzaldehyde (5.0 g, 96%) and *N*-cyclohexyl-*N'*-phenylcarbodiimide (**9e**, 5.7 g, 58%), bp 80° (1 mm), ir (neat) 2140 cm^{-1} (-N=C=N-). The residue was chromatographed (basic aluminum oxide-benzene) to give 1.3 g (82%) of sulfur. The compound **9e** was treated with sodium methoxide in water-methanol to afford *N*-cyclohexyl-*N'*-phenylurea as colorless needles (from EtOH): mp 190-191°; ir (Nujol) 3330 (NH), 1628 (C=O), 1547, 1320, and 1308 cm^{-1} (NH, CN); mass spectrum *m/e* 218 (M^+, calcd 218), 135 ($M^+ - C_6H_{11}$), 119 ($PhNCO^+$).

Anal. Calcd for $C_{13}H_{18}N_2O$: C, 71.53; H, 8.31; N, 12.83. Found: C, 71.31; H, 8.25; N, 12.76.

Under milder conditions, 90° (5.5 hr), the oxaziridine **1e** (11.1 g, 51 mmol, AO 93%) was allowed to react with the isothiocyanate **8** (6.75 g, 50 mmol). The mixture was distilled to give 3.1 g (117%) of benzaldehyde, but none of the carbodiimide **9e**. The residue was chromatographed (basic aluminum oxide-benzene) to give 5.30 g (58%) of 2,4-diphenyl-5-cyclohexylimino-1,2,4-thiadiazolidine-3-thione (**11e**) and 0.03 g (2%) of sulfur. The former was recrystallized from ethanol to give colorless needles: mp 208-209°; ir (Nujol) 1630 cm^{-1} (C=N); mass spectrum *m/e* 367 (M^+, calcd 367), 285 ($M^+ - C_6H_{10}$), 194 ($PhNCNPh^+$), 141 ($C_6H_{11}NCS^+$).

Anal. Calcd for $C_{20}H_{21}N_3S_2$: C, 65.36; H, 5.76; N, 11.43. Found: C, 65.13; H, 5.81; N, 11.31.

Reaction of the Oxaziridine 1b. The reaction of the oxaziridine **1b** (8.0 g, 48 mmol, AO 90%) and the isothiocyanate **8** (10.9 g, 81 mmol) was carried out by the same procedure as above at 85° for 2 hr. The solvent and benzaldehyde (5.1 g, 119%) were distilled off and addition of hexane to the residue precipitated crystalline solid. The solid was filtered and recrystallized (benzene-ethanol) to afford 0.2 g of sulfur and 2.8 g (22%) of 4-ethyl-2-phenyl-5-phenylimino-1,2,4-thiadiazolidine-3-thione (**10b**). The filtrate was chromatographed (basic aluminum oxide-benzene) to give 0.3 g of sulfur and 0.5 g (4%) of 2,4-diphenyl-5-ethylimino-1,2,4-thiadiazolidine-3-thione (**11b**). The combined yield of sulfur was 19%.

10b was obtained as colorless needles (from ethanol-benzene): mp 171-172°; ir (Nujol) 1615 cm^{-1} (C=N); nmr ($CDCl_3$) δ 1.15 (t, 3, J = 6.75 Hz, CH_3), 3.31 (q, 2, J = 6.75 Hz, CH_2), 6.7-7.5 (m, 10, 2 Ph); mass spectrum *m/e* 313 (m^+, calcd 313), 285 ($M^+ - CH_2{=}CH_2$), 226 ($M^+ - EtNCS$), 194 ($PhNCNPh^+$), 178 ($M^+ - PhNCS$), 167 ($M^+ - 146$), 146 ($PhNCNEt^+$), 135 ($PhNCS^+$).

Anal. Calcd for $C_{16}H_{15}N_3S_2$: C, 61.31; H, 4.82; N, 13.41. Found: C, 61.25; H, 4.78; N, 13.35.

11b was obtained as colorless flakes (from ethanol): mp 153-154° ir (Nujol) 1635 cm^{-1} (C=N); nmr ($CDCl_3$) δ 1.29 (t, 3, J = 6.75 Hz, CH_3), 4.03 (q, 2, J = 6.75 Hz, CH_2), 6.7-7.5 (m, 10, 2 Ph); mass spectrum *m/e* 313 (M^+, calcd 313), 285, 225 (285 -

NCS), 194, 178, 167, 145 (PhNCNEt$^+$ − H), 135. Unassigned fragments correspond to those from **10b**.

Anal. Calcd for $C_{16}H_{15}N_3S_2$: C, 61.31; H, 4.82; N, 13.41. Found: C, 61.29; H, 4.83; N, 13.41.

Reaction of the Oxaziridine 1c. From the oxaziridine **1c** (7.3 g, 37 mmol, AO 90%) and the isothiocyanate **8** (5.0 g, 37 mmol), 2.4 g (122%) of benzaldehyde, 0.35 g (30%) of sulfur, 0.50 g (8%) of 4-*n*-butyl-2-phenyl-5-phenylimino-1,2,4-thiadiazolidine-3-thione (**10c**), and 1.75 g (28%) of 2,4-diphenyl-5-*n*-butylimino-1,2,4-thiadiazolidine-3-thione (**11c**) were obtained. The latter three compounds were separated by chromatography.

10c was obtained as pale yellow needles (from ethanol): mp 95–96°; ir (Nujol) 1610 cm^{-1} (C=N); mass spectrum *m/e* 341 (M$^+$, calcd 341), 285 (M$^+$ − EtCH=CH$_2$), 226 (M$^+$ − BuNCS), 206 (M$^+$ − PhNCS), 194 (PhNCNPh$^+$), 174 (PhNCNBu$^+$), 167 (M$^+$ − 174), 135 (PhNCS$^+$).

Anal. Calcd for $C_{18}H_{19}N_3S_2$: C, 63.31; H, 5.61; N, 12.30. Found: C, 63.10; H, 5.53; N, 12.11.

11c was obtained as colorless needles (from ethanol): mp 115–116°; ir (Nujol) 1635 cm^{-1} (C=N); mass spectrum *m/e* 341 (M$^+$, calcd 341), 285, 226, 206, 194, 174, 167, 135. The assignments for these fragments correspond to those for **10c**.

Anal. Calcd for $C_{18}H_{19}N_3S_2$: C, 63.31; H, 5.61; N, 12.30. Found: C, 63.54; H, 5.39; N, 12.16.

Reaction of the Oxaziridine 1d. A mixture of the oxaziridine **1d** (6.5 g, 38 mmol, AO 95%) and phenyl isothiocyanate (**8**, 7.27 g, 54 mmol) in benzene (10 ml) was allowed to react at 90° for 5.5 hr. Removal of the solvent precipitated 1.5 g of 4-isopropyl-2-phenyl-5-phenylimino-1,2,4-thiadiazolidine-3-thione (**10d**). The filtrate was distilled to give 2.8 g (97%) of benzaldehyde and small amounts of **1d** and **8**. The residue was chromatographed (basic aluminum oxide–benzene) to give 1.6 g of the compound **10d** and 0.1 g (1%) of 2,4-diphenyl-5-isopropylimino-1,2,4-thiadiazolidine-3-thione (**11d**). The total yield of the compound **10d** was 3.1 g (36%).

10d was obtained as colorless needles (from ethanol): mp 166.5–167°; ir (Nujol) 1612 cm^{-1} (C=N); nmr (CDCl$_3$) δ 1.07 (d, 6, J = 6.5 Hz, 2 CH$_3$), 3.4 (m, 1, J = 6.5 Hz, CH), 6.7–7.5 (m, 10, 2 Ph); mass spectrum *m/e* 327 (M$^+$, calcd 327), 285 (M$^+$ − MeCH=CH$_2$), 226 (M$^+$ − PrNCS), 194 (PhNCNPh$^+$), 192 (M$^+$ − PhNCS), 167 (M$^+$ − 160), 160 (PhNCNPr$^+$), 150 (285 − 135), 135 (PhNCS$^+$), 101 (PrNCS$^+$).

Anal. Calcd for $C_{17}H_{17}N_3S_2$: C, 62.35; H, 5.23; N, 12.83. Found: C. 62.20; H, 5.17; N, 12.89.

11d was obtained as colorless needles (from ethanol): mp 196.5–197°; ir (Nujol) 1635 cm^{-1} (C=N); nmr (CDCl$_3$) δ 1.37 (d, 6, J = 6.6 Hz, 2 CH$_3$), 5.4 (m, 1, J = 6.6 Hz, CH), 6.8–7.8 (m, 10, 2 Ph); mass spectrum *m/e* 327 (M$^+$, calcd 327), 285, 226, 194, 192, 167, 160, 150, 135, 101. These fragments correspond to those from **10d**.

Anal. Calcd for $C_{17}H_{17}N_3S_2$: C, 62.35; H, 5.23; N, 12.83. Found: C, 62.63; H, 5.15; N, 12.68.

Reaction of the Oxaziridine 1f. The oxaziridine **1f** (8.13 g, 46 mmol, AO 98%) and the isothiocyanate **8** (6.2 g, 46 mmol) were allowed to react at 105° for 2 hr. Then the mixture was cooled to give a quantitative amount (14.5 g) of crystalline solid. A part (3.0 g) of the filtered solid was chromatographed (basic aluminum oxide–benzene) and 2.04 g (62%) of 2-*tert*-butyl-3,4-diphenyl-1,2,4-oxadiazolidine-5-thione (**12**) and 0.57 g (19%) of 2-*tert*-butyl-3,4-diphenyl-1,2,4-oxadiazolidin-5-one (**13**) were obtained. The filtrate was proved to contain small amounts of benzaldehyde and *N,N'*-di-*tert*-butylcarbodiimide by ir and glpc. The oxadiazolidinethione **12** was recrystallized from ethanol to afford colorless needles: mp 129–130°; ir (Nujol) 1295 and 1157 cm^{-1}; nmr (CCl$_4$) δ 1.32 (s, 9, *t*-Bu), 5.93 (s, 1, CH), 7.1–7.4 (m, 10, 2 Ph); mass spectrum *m/e* 312 (M$^+$, calcd 312), 252 (M$^+$ − COS), 180 (PhN=CPh$^+$), 161 (PhCH=NBu-*t*$^+$).

Anal. Calcd for $C_{18}H_{20}NOS$: C, 69.19; H, 6.45; N, 8.97. Found: C, 69.27; H, 6.39; N, 8.95.

The oxadiazolidinone **13** was identical with an authentic sample.[1]

Reaction of the Oxaziridine 1i. A solution of the oxaziridine **1i** (2.05 g, 6.5 mmol, AO 93%) and the isothiocyanate **8** (1.22 g, 9.0 mmol) in toluene (10 ml) was refluxed for 7 hr. The ir spectrum of the mixture showed the strong absorption of unreacted **8** and no absorption of the benzoyl group. The mixture was distilled to give 0.65 g of **8** and 1.08 g (53%) of 2,2-pentamethylene-5-phenyl-1,3,4-dioxazoline, which is reported in the preceding paper.[1]

Reaction of the Oxaziridine 1k. The reaction between the oxaziridine **1k** (12.7 g, 50 mmol, AO 83%) and the isothiocyanate **8** (6.7 g, 50 mmol) at 100° for 1.4 hr gave 3.8 g (143%) of benzaldehyde, 1.05 g (67%) of sulfur, and 0.65 g (7%) of 2-phenyl-4-benzyl-5-phenylimino-1,2,4-thiadiazolidine-3-thione (**10k**). The last compound was recrystallized from benzene–ethanol to give pale yellow needles: mp 151.5–153.5°; ir (Nujol) 1612 cm^{-1} (C=N); mass spectrum *m/e* 375 (M$^+$, calcd 375), 343 (M$^+$ − S), 240 (M$^+$ − PhNCS), 208 (PhNCNCH$_2$Ph$^+$), 167 (M$^+$ − 208), 135 (PhNCS$^+$).

Anal. Calcd for $C_{21}H_{17}N_3S_2$: C, 67.17; H, 4.56; N, 11.19. Found: C, 66.89; H, 4.56; N, 10.99.

Pyrolysis of the Thidiazolidinethione 10d. The compound **10d** (800 mg, 2.45 mmol) was heated at 180–190° (10 mm) in an apparatus equipped with a trap cooled with Dry Ice. The trapped liquid (600 mg) was identified and determined by glpc to contain 165 mg (25%) of phenyl isothiocyanate, 84 mg (34%) of isopropyl isothiocyanate, and 99 mg (26%) of *N*-isopropyl-*N'*-phenylcarbodiimide. From the residue, 95 mg (61%) of sulfur was obtained.

Treatment of the Compound 10d with Triethyl Phosphite. The thiadiazolidinethione **10d** (1.0 g, 3.1 mmol) and triethyl phosphite (50 mg, 0.31 mmol) in benzene (7 ml) was refluxed for 1 hr. The solvent was removed *in vacuo* and the residue was solidified. Recrystallization (ethanol) gave 610 mg (61%) of the rearranged product **11d**.

When the compound **10d** (500 mg, 1.5 mmol) was treated with the phosphite (300 mg, 1.8 mmol) in benzene under similar conditions, an ir spectrum of the mixture indicated the formation of an isothiocyanate (*ca.* 2120 cm^{-1}). The mixture was distilled and determined by glpc; phenyl isothiocyanate (42 mg, 17%), isopropyl isothiocyanate (30 mg, 17%), and triethyl thiophosphite (226 mg, 64%) were obtained. The residue showed the ir absorptions of a carbodimide (2150 cm^{-1}) and the rearranged product **11d**. The treatment of the residue with water gave 21 mg of *N,N'*-diphenylurea, which showed the formation of *N,N'*-diphenylcarbodiimide (7%) and 15 mg (3%) of **11d**.

Hydrolysis of the Compound 10d. To a solution of the compound **10d** (400 mg, 1.2 mmol) in ethanol (15 ml), 3 ml of 12 *N* hydrochloric acid was added and the solution was refluxed for 5 hr, extracted (ether), dried (Na$_2$SO$_4$), and concentrated. The resultant solid was recrystallized (methanol) to give 190 mg (87%) of *N*-isopropyl-*N'*-phenylurea, which was identical with an authentic sample from phenyl isocyanate and isopropylamine.

Reduction of the Thiadiazolidinethione 10d. The compound **10d** (500 mg, 1.5 mmol) was treated with LiAlH$_4$ (1.0 g) in refluxing ether for 5 hr, followed by hydrolysis, extraction (ether), drying (Na$_2$SO$_4$), and concentration. The resultant solid was recrystallized (ethanol–benzene) to give 110 mg (32%) of *N,N'*-diphenylthiourea, which was identical with an authentic sample.

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Registry No.—**1a,** 3400-12-2; **1b,** 7771-15-5; **1c,** 21710-99-6; **1d,** 7731-32-0; **1e,** 21711-00-2; **1f,** 7731-34-2; **1g,** 21711-01-3; **1i,** 2289-83-0; **1j,** 3400-13-3; **1k,** 7731-37-5; **2,** 75-15-0; butyl isothiocyanate, 592-82-5; *N,N'*-dicyclohexylthiourea, 1212-29-9; phenyl isothiocyanate, 103-72-0; **9e,** 3878-67-9; **10a,** 50506-86-0; **10b,** 50506-87-1; **10c,** 50506-88-2; **10d,** 50506-89-3; **10k,** 50506-90-6; **11b,** 50506-91-7; **11c,** 50506-92-8; **11d,** 50506-93-9; **11e,** 50506-94-0; **12,** 50506-95-1; **13,** 50506-96-2; *N,N'*-di-*n*-butylthiourea, 109-46-6; α-phenyl-*N*-*tert*-butylnitrone, 3376-24-7; *N*-cyclohexyl-*N'*-phenylurea, 886-59-9.

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Nitrile Sulfides. Synthesis of 1,2,4-Thiadiazoles

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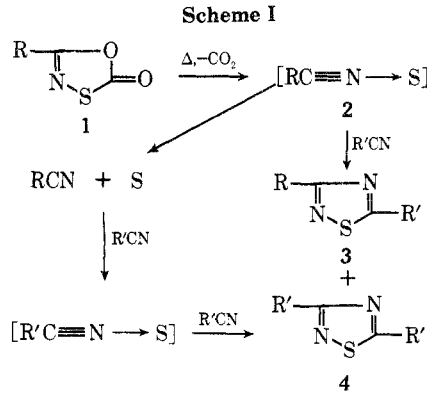
Reaction of nitriles with nitrile sulfide intermediates, generated by thermolysis of 1,3,4-oxathiazol-2-ones, resulted in 1,2,4-thiadiazoles. The scope of this new synthesis of thiadiazoles was explored; highest yields are obtained with electrophilic nitriles and with aromatic nitrile sulfides.

1,3-Dipolar cycloaddition reactions of nitrile oxides have been employed repeatedly in syntheses of heterocyclic compounds.[1,2] Until recently,[3,4] nitrile sulfides have been unavailable for syntheses of N–S heterocycles *via* cycloadditions. We have provided evidence that nitrile sulfides may be generated as reactive intermediates by thermolysis of 1,3,4-oxathiazol-2-ones and may be trapped in 1,3-dipolar cycloaddition reactions with acetylenes such as dimethyl acetylenedicarboxylate and ethyl propiolate.[3,4] We report here a new synthesis of 1,2,4-thiadiazoles *via* cycloaddition of nitrile sulfides to nitriles.

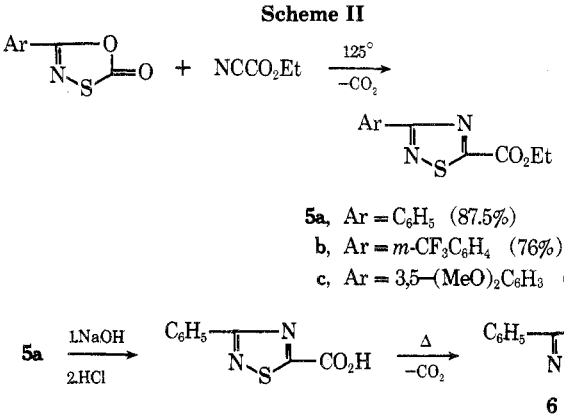
Thermolysis of 5-substituted 1,3,4-oxathiazol-2-ones (**1**) in excess nitrile led to thiadiazoles **3** and, in several cases, to lesser amounts of by-products **4** (Scheme I, Table I). Competitive decomposition of the intermediate nitrile sulfides produced sulfur and the nitrile derived from the oxathiazolone. Although the thiadiazole reaction proceeds less readily than the analogous 1,3-dipolar cycloaddition of nitrile oxides to nitriles to give 1,2,4-oxadiazoles,[5,6] under certain conditions reasonable yields of thiadiazoles may be obtained (Tables I and II). Thus, decarboxylation of 5-phenyl-1,3,4-oxathiazol-2-one in 35 equiv of benzonitrile at 190° gave 3,5-diphenyl-1,2,4-thiadiazole in 50% yield. The product and authentic material, prepared by iodine oxidation of thiobenzamide,[7] gave identical ir spectra and gave an undepressed mixture melting point. Products **3** and **4** were further characterized by mass spectrometry; the major fragmentation routes result in loss of RCN and R′CN (see Experimental Section), as found previously[8] for 3,5-disubstituted 1,2,4-thiadiazoles.

Scheme I



The cycloadditions of aromatic nitrile sulfides to ethyl cyanoformate proceeded especially well to give the ethyl 3-aryl-1,2,4-thiadiazole-5-carboxylates **5a**, **5b**, and **5c** (Scheme II; the indicated yields are for isolated pure products). Hydrolysis of **5a** and decarboxylation of the resultant acid gave the known[9] 3-phenyl-1,2,4-thiadiazole (**6**) in 99% yield.

Scheme II



By-product **4** (Scheme I) probably occurs *via* cycloaddition of R′CNS to R′CN. The R′CNS could form from reaction of atomic sulfur with R′CN[10] (Scheme I) or from direct sulfur atom transfer between RCNS and R′CN. Yields of **3** were found to increase with greater excesses of nitrile, as expected, and with higher temperatures (Tables I and II). Evidently, the rate of cycloaddition reaction to form thiadiazole increases more rapidly with temperature than the competing decomposition of nitrile sulfide to nitrile and sulfur. The data of Table I reveal that the yields of thiadiazoles increase with more electrophilic nitriles and decrease with less electrophilic nitriles.[11] Substituent effects in the oxathiazolones are similar. Because the yield of cycloaddition product **3** depends on the relative rates of cycloaddition and decomposition of the substituted nitrile sulfide, the absolute effects of substituents in the oxathiazolones on the cycloaddition rate are not readily determined. Thermolysis of 5-phenyl-1,3,4-oxathiazol-2-one at 125° in chlorobenzene in the presence of 1 equiv of boron trifluoride etherate showed an eightfold rate enhancement, but the presence of boron trifluoride etherate resulted in lower yields of thiadiazole (Table II) in the cycloaddition reaction.[12]

Our new synthesis of 1,2,4-thiadiazoles allows ready preparation of 3,5-unsymmetrically substituted derivatives with no uncertainty about the position of the substituents. Thus, both 3-phenyl-5-*p*-tolyl-1,2,4-thiadiazole, mp 115–116°, and 5-phenyl-3-*p*-tolyl-1,2,4-thiadiazole, mp 77.5–79°, were prepared unambiguously. A previous report[13] of the preparation of 3- (or 5-) phenyl-5- (or 3-) *p*-tolyl-1,2,4-thiadiazole, mp 56°, did not allow an exact