1,2,3-Thiadiazoles. I. Synthesis of Sodium (or Potassium) 1,2,3-Thiadiazole-4-thiolates *via* Thiocarbazonate Esters and *N*-Acylthiohydrazonate Esters

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A general synthesis of 1,2,3-thiadiazole-4-thiolates **1** and their derivatives **2-3** by an extension of the Hurd-Mori 1,2,3-thiadiazole synthesis is described. Treatment of methyl (or ethyl) [1-(alkylthio)alkylidene]hydrazinocarboxylates **11** (thiocarbazonate esters) or other *N*-acylthiohydrazonate esters [Y = ureido (**12**) or arenesulfonyl (**13**)] with thionyl chloride affords **2-3** efficiently. Intermediates **11-13** are readily obtained from the N^2-thioacylcarbazates **8**, N^3-thioacylsemicarbazides **9**, or N^2-thioacyl-N^1-(*p*-toluenesulfonyl)hydrazides **10**, respectively, by *S*-alkylation. Physicochemical properties of the 1,2,3-thiadiazoles **1-3** and *N*-acylthiohydrazonate esters **11-13** are also described.

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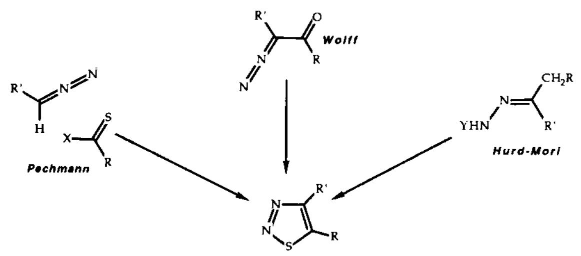
Since the initial report by von Pechmann and Nold describing the synthesis and characterization of a 1,2,3-thiadiazole [1], there has been limited research on this rarest of the isomeric thiadiazoles. Early chemical investigations of the 1,2,3-thiadiazole nucleus have yielded information concerning its theoretical and physical chemical properties [2,3]; more recently, researchers have reported on the potential synthetic utility of 1,2,3-thiadiazoles for highly reactive intermediates (*e.g.* thioketenes [4] and alkynethiolate salts [5]), other heterocycles [6], and mesoionic derivatives [7]. With the recent discovery of several biologically active agents incorporating the 1,2,3-thiadiazole moiety [8], emphasis has been placed on the development of general syntheses of functionalized 1,2,3-thiadiazoles [9].

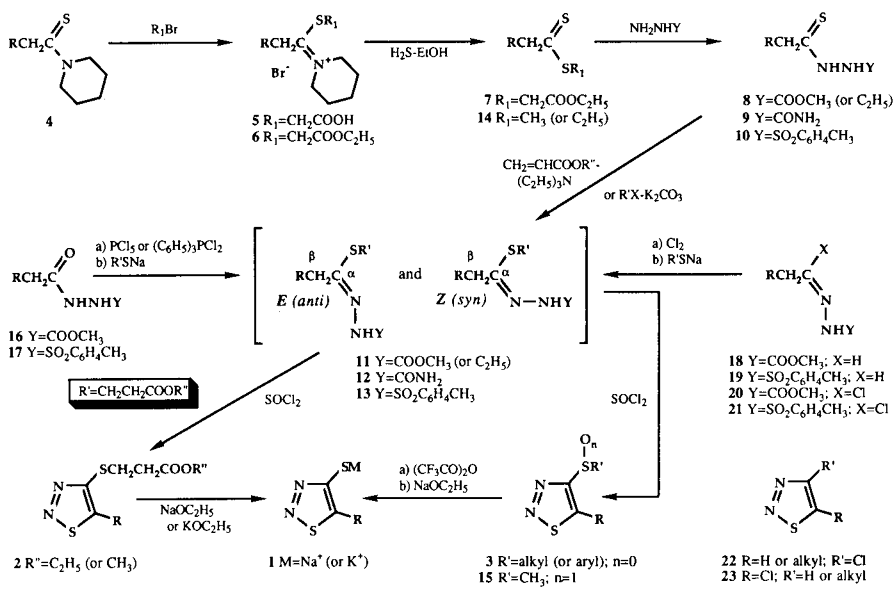
With the exception of specialized syntheses involving the rearrangement of other heterocyclic systems [6b,10], two classes of synthetic approaches to mononuclear 1,2,3-thiadiazoles are known. These are classified as "diazo" and "non-diazo" approaches. The "diazo" approaches based on either a) the [3+2] dipolar cycloaddition of diazoalkanes to isothiocyanates [1,6c,11] or other thiocarbonyl components [11] (modified Pechmann synthesis) or b) the thionation of α-diazoketones [12] (Wolff synthesis) are infrequently utilized due to the inherent hazards. Often the cycloadditions are also complicated by the lack of regiospecificity [13]. The method of choice, a convenient "non-diazo" approach, developed by Hurd and Mori involves the oxidative cyclization of *N*-acylhydrazones with thionyl chloride, but no detailed mechanistic study was reported subsequently [14]. Subsequently this reaction was utilized by Raap and Micetich for the synthesis of 4-aryl-1,2,3-thiadiazoles [15]. In principle, numerous 1,2,3-thiadiazoles could be realized with the Hurd-Mori synthesis by substituent variations in the starting *N*-acylhydrazones [16].



As part of a synthetic investigation we required a facile, regiospecific synthesis for the unreported 1,2,3-thiadiazole-4-thiolates **1**. Conceptually, at least, the presence of the 4-thiolate substituent in **1** suggested that extension of the Hurd-Mori cyclization to methyl (or ethyl) [1-(alkylthio)alkylidene]hydrazinocarboxylates **11** (henceforth referred to as thiocarbazonate esters) or other *N*-acylthiohydrazonate esters [Y = ureido (**12**) or arenesulfonyl (**13**)] [17], *in lieu* of *N*-acylhydrazones, might be an attractive approach to **1**. The thiocarbazonate esters **11** could be obtained by *S*-alkylation of the appropriate N^2-(thioxoalkyl)-carbazates (or N^2-thioacylcarbazates) **8**, obtainable by thioacylation of methyl (or ethyl) hydrazinocarboxylate. Thus various C-5 and *S*-alkyl (or *S*-aryl) substituents could be introduced into the 1,2,3-thiadiazole nucleus (Scheme I).

The synthesis of the requisite N^2-thioacylcarbazates **8**, N^3-thioacylsemicarbazides **9**, or N^2-thioacyl-N^1-arenesulfonylhydrazides **10** begins with thioacylation of methyl (or ethyl) hydrazinocarboxylate, semicarbazide, or an arenesulfonylhydrazide, respectively, with *S*-thioacylthioglycolate esters **7** [18]. In contrast to the reported lability of thiohydrazides [19], the desired N^2-thioacyl-N^1-acylhydrazides **8-10** are thermally stable and easily purified by chromatography over magnesium trisilicate or silica gel (Table I and II). The thioacylation agents **7** were prepared by sulfhydrolysis (hydrogen sulfide-ethanol) of the

Scheme I



S-carboxymethylthiopiperidium bromides (or iodides) **5-6**, obtained from *N*-thioacylpiperidides **4**, by a modification of the procedure of Jensen and Pedersen [20].

While preparation of **8-10** was accomplished readily from *S*-thioacylthioglycolate esters **7**, a more expedient synthesis of **8-10** was desired. Similarly, treatment of the readily available methyl (or ethyl) dithioalkanoates **14** with methyl hydrazinocarboxylate afforded mixtures of the thiocarbazonate esters **11** (major component) and the desired N^2-thioacylcarbazates **8** [21,22]. Modification of the reaction conditions had minimal effect on the ratios of **11:8**, but preference for formation of the *Z*(syn)-thiocarbazonate esters **11Z** was consistently observed (*vide infra*). Since the N^2-thioacylcarbazates **8** are sufficiently acidic (*cf.* Experimental), separation of **8** from **11** was accomplished efficiently be extraction with aqueous alkali. Acidification then afforded **8** in a pure state (>95%), as determined by proton magnetic resonance spectroscopy and infrared spectral analyses. Similar results were also observed with semicarbazide and *p*-toluenesulfonylhydrazide.

With **8-10** in hand, the *S*-alkylation of these intermediates was then explored. The alkylation of **8-10**, under thermodynamic conditions, occurred exclusively on sulfur with various alkylating agents (*e.g.* allyl bromide, benzyl bromide, 2,4-dinitrofluorobenzene, iodomethane, methyl bromoacetate) to yield *E*(anti)/*Z*(syn)-isomeric mixtures of the requisite esters **11-13** in excellent yields (>85%) with a preponderance of the *Z*(syn)-isomers [*Z*(syn): *E*(anti) = 40 to 3:1] (*vide infra*). Separation of the isomers could be accomplished by hplc, on silica gel; in general, with each pair of isomers, the least polar component was the *Z*(syn)-isomer. In several cases the crystalline *Z*(syn)-thiocarbazonate esters (**11Za-11Zb, 11Zp**) were easily separated from the corresponding oily *E*(anti)-isomers by fractional crystallization. Generally the isomer mixtures were utilized in the subsequent cyclization without separation of the isomers.

The proton nuclear magnetic resonance spectra of the *E*(anti) and *Z*(syn)-isomers of **11-13** revealed significant differences between the isomeric pairs. In the absence of appropriate models for the thiocarbazonate esters, it was initially not possible to ascertain unambiguously the relative position of the nitrogen and sulfur atoms with respect to the carbon-nitrogen double bond. Structural

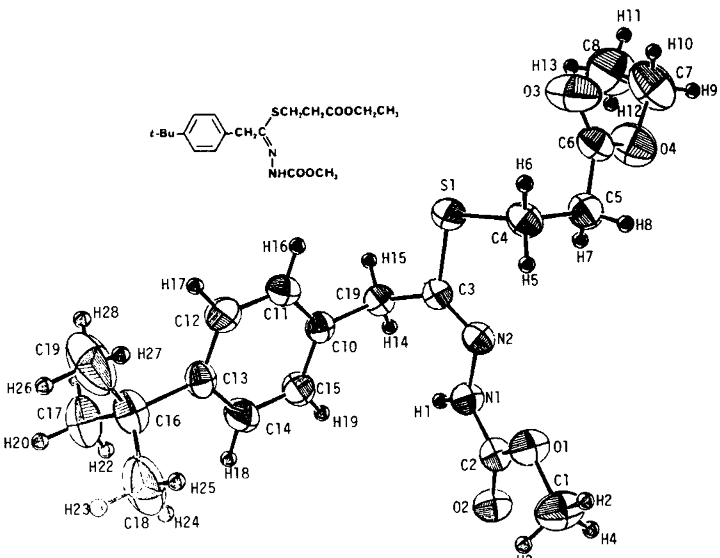
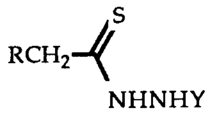


Figure 1. X-Ray crystal structure of thiocarbazonate ester **11Ef**

Table I

Physical Constants of N^2-Thioacylcarbazates **8**, N^3-Thioacylsemicarbazides **9**, N^2-Thioacylarylsulfonylhydrazides **10**



Compound	R	Y	Yield, %	Mp, °C	Formula	Analysis (Calcd./Found) C	H	Cl(F)	N	S
8a	H	CH_3O_2C	75	ivory crystals	$C_4H_8N_2O_2S$	32.42	5.44		18.90	21.64
				99.0-100.5° [a]		32.68	5.27		19.23	21.31
8b	H	$C_2H_5O_2C$	79	ivory crystals	$C_5H_{10}N_2O_2S$	37.02	6.21		17.27	19.76
				54.0-57.5° [b]		36.82	6.11		17.47	19.71
8c	*t*-butyl	CH_3O_2C	81	ivory crystals	$C_8H_{16}N_2O_2S$	47.04	7.89		13.71	15.69
				72.5-73.0° [b]		47.18	7.84		13.87	15.98
8d	C_6H_5	CH_3O_2C	85	yellow crystals	$C_{10}H_{12}N_2O_2S$	53.55	5.39		12.49	14.29
				93.5-94.0° [c]		53.76	5.20		12.52	14.29
8e	4-$CH_3C_6H_4$	CH_3O_2C	91	ivory crystals	$C_{11}H_{14}N_2O_2S$	55.44	5.92		11.76	13.45
				104.5-105.5° [d]		55.57	5.87		11.75	13.50
8f	4-*t*-BuC_6H_4	CH_3O_2C	97	ivory crystals	$C_{14}H_{20}N_2O_2S$	59.97	7.19		9.99	11.43
				93.0-94.0° [b]		60.27	7.29		9.96	11.17
8g	4-$CH_3OC_6H_4$	CH_3O_2C	81	yellow crystals	$C_{11}H_{14}N_2O_3S$	51.95	5.55		11.02	12.61
				94.5-95.0° [d]		52.14	5.81		11.25	12.58
8h	3,4,5-$(CH_3O)_3C_6H_2$	CH_3O_2C	85	ivory crystals	$C_{13}H_{18}N_2O_5S$	49.67	5.77		8.91	10.20
				133.5-134.0° [c]		49.51	5.59		9.12	10.17
8i	2-naphthyl	CH_3O_2C	89	yellow crystals	$C_{14}H_{14}N_2O_2S$	61.29	5.14		10.21	11.69
				129.0-131.0° [c]		61.46	5.12		10.23	11.50
8j	2-thienyl	CH_3O_2C	75	yellow crystals	$C_8H_{10}N_2O_2S_2$	41.72	4.38		12.16	27.84
				74.0-75.0° [e]		41.87	4.31		12.32	28.08
8k	4-ClC_6H_4	CH_3O_2C	78	ivory crystals	$C_{10}H_{11}ClN_2O_2S$	46.43	4.29	13.70	10.82	12.39
				147.5-148.0° [c]		46.39	4.25	13.78	10.90	12.34
8l	4-FC_6H_4	CH_3O_2C	80	ivory crystals	$C_{10}H_{11}FN_2O_2S$	49.58	4.58	7.84	11.56	13.23
				149.5-151.5° [c]		49.80	4.59	8.05	11.61	13.35
8m	3-$CH_3OC_6H_4$	CH_3O_2C	96	ivory crystals	$C_{11}H_{14}N_2O_3S$	51.95	5.55		11.02	12.61
				56.0-58.0° [c]		51.80	5.50		11.07	12.75
8n	3-$CF_3C_6H_4$	CH_3O_2C	96	yellow crystals	$C_{11}H_{11}F_3N_2O_2S$	45.20	3.79	19.50	9.58	10.97
				131.0-132.5° [c]		45.38	3.80	19.25	9.96	11.15
8o	$C_2H_5O_2C$	CH_3O_2C	60	yellow oil	$C_7H_{12}N_2O_4S$	38.18	5.49		12.72	14.56
						38.05	5.35		12.85	14.48
8p	C_6H_5S	CH_3O_2C	65	yellow oil	$C_{10}H_{12}N_2O_2S_2$	46.86	4.72		10.93	25.01
						46.73	4.73		10.79	24.99
8q	2-Tetrahydro-	CH_3O_2C	85	ivory crystals	$C_9H_{16}N_2O_3S$	46.53	6.94		12.06	13.80
	pyranyl			109.5-110.5° [f]		46.46	6.99		12.10	14.06
9a	$C_6H_5CH_2$	NH_2CO	85	white crystals	$C_{10}H_{13}N_3OS$	53.79	5.87		18.82	14.36
				118.0-119.0° [c]		53.92	5.73		19.16	14.48
9b	CH_3	NH_2CO	65	white crystals	$C_4H_9N_3OS$	32.64	6.16		28.55	21.78
				136.0-137.0° [g]		32.52	5.92		28.56	21.90
9c	C_2H_5	NH_2CO	70	white crystals	$C_5H_{11}N_3OS$	37.25	6.88		26.06	19.89
				134.5-136.0° [g]		37.20	6.71		26.03	19.88
10a	H	4-$CH_3C_6H_4SO_2$	80	white crystals	$C_9H_{12}N_2O_2S_2$	44.24	4.95		11.47	26.25
				136.5-137.0° [f]		44.10	5.00		11.29	26.09
10b	CH_3	4-$CH_3C_6H_4SO_2$	85	white crystals	$C_{10}H_{14}N_2O_2S_2$	46.44	5.46		10.84	24.82
				83.5-84.5° [f]		46.40	5.38		10.65	24.53

[a] Toluene-methylcyclohexane. [b] Methylcyclohexane. [c] Toluene. [d] Toluene-hexane. [e] Methylcyclohexane-diisopropyl ether (9:1). [f] *t*-Butyl methyl ether. [g] Ethanol-ethyl acetate.

assignments for several prototypical thiocarbazonate esters (**11Ef** and **11Zu**) were determined unequivocally by single crystal X-ray analyses. The ORTEP drawings are presented in Figures 1 and 2. Correlations of the proton magnetic spectra and isomeric structures could then be obtained. Routinely, structural assignments could be made based on the relative chemical shifts of the methylene unit (β-carbon) for isomeric pairs of esters **11-13**. For

Table II

Spectroscopic Properties of N^2-Thioacyl-N^1-acylhydrazides **8-10**

Compound	^{1}H NMR (δ [ppm], deuteriochloroform) [a]
8a	2.42 (s, 3H, CH_3CS), 3.76 (s, 3H, OCH_3), 8.55 (bs, 1H, NH), 9.56 (bs, 1H, NH)
8b	1.30 (t, 3H, J = 7.4 Hz, CH_3CH_2), 2.55 (s, 3H, CH_3CS), 4.25 (q, 2H, CH_2CH_3), 8.75 (bs, 1H, NH), 10.35 (bs, 1H, NH)
8c	1.07 (s, 9H, *t*-butyl), 2.63 (s, 2H, CH_2CS), 3.80 (s, 3H, OCH_3), 8.75 (bs, 1H, NH), 9.65 (bs, 1H, NH)
8d	3.79 (s, 3H, OCH_3), 4.11 (s, 2H, CH_2CS), 7.33 (bs, 5H, C_6H_5), 8.65 (bs, 1H, NH), 9.55 (bs, 1H, NH)
8e	2.38 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 4.07 (s, 2H, CH_2CS), 7.23 (s, 4H, C_6H_4), 8.68 (bs, 1H, NH), 9.52 (bs, 1H, NH)
8f	1.30 (s, 9H, *t*-butyl), 3.74 (s, 3H, OCH_3), 4.04 (s, 2H, CH_2CS), [7.20 (d, 2H, J = 8.0 Hz) and 7.38 (d, 2H) (C_6H_4)], 8.54 (bs, 1H, NH), 9.35 (bs, 1H, NH)
8g	3.78 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.03 (s, 2H, CH_2CS), [6.89 (d, 2H, J = 8.2 Hz) and 7.21 (d, 2H) (C_6H_4)], 8.60 (bs, 1H, NH), 9.40 (bs, 1H, NH)
8h	3.77 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.87 [s, 6H, OCH_3 (2 x)], 4.04 (s, 2H, CH_2CS), 6.52 (s, 2H, H arom), 8.51 (bs, 1H, NH), 9.15 (bs, 1H, NH)
8i	3.75 (s, 3H, OCH_3), 4.27 (s, 2H, CH_2CS), 7.30-8.00 (m, 7H, H arom), 8.55 (bs, 1H, NH), 9.50 (bs, 1H, NH)
8j	3.79 (s, 3H, OCH_3), 4.30 (s, 2H, CH_2CS), [7.00 (m, 2H) and 7.30 (m, 1H) (H arom)], 8.65 (bs, 1H, NH), 9.72 (bs, 1H, NH)
8k	3.80 (s, 3H, OCH_3), 4.03 (s, 2H, CH_2CS), 7.31 (bs, 4H, C_6H_4), 8.60 (bs, 1H, NH), 9.90 (bs, 1H, NH)
8l	3.77 (s, 3H, OCH_3), 4.03 (s, 2H, CH_2CS), [7.10 (dd, 2H, $^3J_{H-F}$ = 8.5 Hz, 8.5 Hz) and 7.30 (dd, 2H, $^4J_{H-F}$ = 6.0 Hz) (C_6H_4)], 8.60 (bs, 1H, NH), 9.60 (bs, 1H, NH)
8m	3.78 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 4.04 (s, 2H, CH_2CS), [6.90 (m, 3H) and 7.30 (dd, 1H, J = 8.0 Hz, 8.0 Hz) (C_6H_4)], 8.65 (bs, 1H, NH), 9.80 (bs, 1H, NH)
8n	3.80 (s, 3H, OCH_3), 4.10 (s, 2H, CH_2CS), 7.55 (m, 4H, C_6H_4), 8.55 (bs, 1H, NH), 9.90 (bs, 1H, NH)
8o	1.30 (t, 3H, CH_3CH_2O), 3.87 (s, 3H, OCH_3), 3.91 (s, 2H, CH_2CS), 4.27 (q, 2H, OCH_2CH_3), 8.85 (bs, 1H, NH), 11.52 (bs, 1H, NH)
8p	3.79 (s, 3H, OCH_3), 4.18 (s, 2H, SCH_2CS), 7.32 (bs, 5H, C_6H_5), 8.55 (bs, 1H, NH), 10.55 (bs, 1H, NH)
8q	[b] 1.35-1.85 [m, 6H, $(CH_2)_3CH_2O$], 2.92 (m, 2H, $CHCH_2CS$), 3.55 (m, 2H, CH_2O), 3.79 (s, 3H, OCH_3), 4.10 (m, 1H, $CHCH_2$), 8.72 (bs, 1H, NH), 10.98 (bs, 1H, NH)
9a	2.95 (m, 2H, CH_2), 3.12 (m, 2H, CH_2), 4.79 (bs, 2H, NH_2), 7.28 (bs, 5H, C_6H_5), 8.83 (bs, 1H, NH), 9.75 (bs, 1H, NH)
9b	1.20 (t, 3H, J = 7.4 Hz, CH_3), 2.60 (q, 2H, CH_2CS), 5.70 (bs, 2H, NH_2), 9.33 (bs, 1H, NH), 11.33 (bs, 1H, NH)
9c	0.95 (t, 3H, J = 7.5 Hz, CH}), 1.80 (m, 2H, CH_2CH_3), 2.64 (t, 2H, J = 7.4 Hz, CH_2CS), 5.85 (bs, 2H, NH_2), 9.27 (bs, 1H, NH), 11.27 (bs, 1H, NH)
10a	2.37 (s, 3H, CH_3), 2.43 (s, 3H, aryl-CH_3), [7.30 (d, 2H, J = 8.3 Hz) and 7.80 (d, 2H) (C_6H_4)], 9.50 [bs, 2H, NH (2 x)]
10b	1.13 (t, 3H, J = 7.5 Hz, CH_3CH_2), 2.43 (s, 3H, aryl-CH_3), 2.57 (q, 2H, CH_2CH_3), [7.30 (d, 2H, J = 8.3 Hz) and 7.80 (d, 2H) (C_6H_4)], 9.50 [bs, 2H, NH (2 x)]

[a] 90 MHz. [b] 300 MHz.

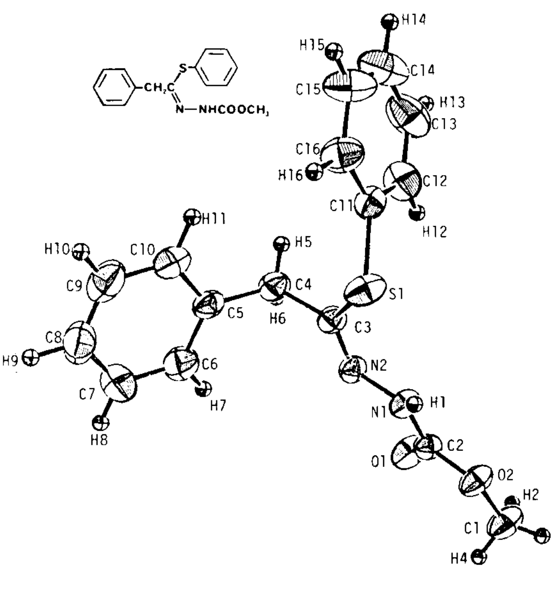


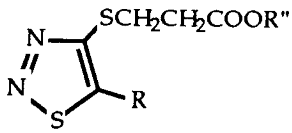
Figure 2. X-Ray crystal structure of thiocarbazonate ester **11Zu**

esters with aromatic substituents on the β-carbon and an alkoxycarbonylethyl substituent (or alkoxycarbonylmethyl, cyanoethyl, cyanomethyl, or aromatic) on the sulfur, the chemical shifts of the methylene group (β-carbon) in the *Z*(syn)-isomers was always downfield of that for the corresponding *E*(anti)-isomers (Class I). In contrast, for thiohydrazonate esters, not satisfying the above structural features, the shifts of the methylene group for the *Z*(syn)-isomer were upfield of that for the corresponding *E*(anti)-isomers (Class II, *e.g.* **11q-11t**).

At this juncture in the synthesis of **1**, the *S*-alkyl unit serves a crucial function as a thiol protecting group for the 1,2,3-thiadiazoles. We anticipated that the 1,2,3-thiadiazole-4-thiolates **1** would be more stable then the corresponding thiols by analogy to the reported physical chemical properties of potassium 1,2,3-thiadiazole-5-thiolate [23]. Accordingly, the optimal *S*-alkyl unit should satisfy two constraints- a) stability to the acidic cyclization conditions and b) ease of removal to yield the thiolate salts directly. The 3-alkoxycarbonylethylthio protecting group was selected for its ease of incorporation into **8-10** (ethyl acrylate, organic base catalyst or ethyl 3-iodopropionate, anhydrous potassium carbonate) and presumed ease of removal from **2** [metal alkoxides or 1,5-diazabicyclo[5.4.0]-undec-5-ene (DBU)]. Subsequently, the majority of the synthetic studies were performed with the 3-alkoxycarbonylethylthio functionality.

Table III

Physical Constants of Ethyl (or Methyl) 3-(1,2,3-Thiadiazol-4-ylthio)propionates **2**



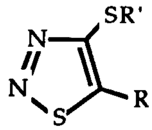
Compound	R	R''	Yield, % [a]	Mp, °C	Formula	Analysis (Calcd./Found) C	H	Cl(F)	N	S
2a	H	CH_3	50 (A)	light yellow oil	$C_6H_8N_2O_2S_2$	35.28	3.95		13.71	31.40
						35.10	4.00		13.55	31.35
2b	H	C_2H_5	50 (A)	light yellow oil	$C_7H_{10}N_2O_2S_2$	38.52	4.62		12.83	29.37
			60 (C)			38.34	4.55		12.78	29.55
2c	CH_3	C_2H_5	50 (B)	light yellow oil	$C_8H_{12}N_2O_2S_2$	41.36	5.21		12.05	27.60
			65 (C)			41.27	5.30		12.00	27.75
2d	C_2H_5	C_2H_5	65 (B)	light yellow oil	$C_9H_{14}N_2O_2S_2$	43.88	5.73		11.37	26.03
						44.01	5.64		11.25	25.99
2e	*t*-butyl	CH_3	67 (A) [b]	light yellow oil	$C_{10}H_{16}N_2O_2S_2$	46.13	6.19		10.76	24.63
						45.94	6.08		10.47	24.34
2f	*t*-butyl	C_2H_5	60 (A) [b]	light yellow oil	$C_{11}H_{18}N_2O_2S_2$	48.15	6.61		10.21	23.36
						48.05	6.55		10.16	23.05
2g	C_6H_5	C_2H_5	95 (A)	white cubes	$C_{13}H_{14}N_2O_2S_2$	53.05	4.80		9.52	21.78
				57.5-58.5° [c]		53.09	4.69		9.46	21.77
2h	4-$CH_3C_6H_4$	C_2H_5	80 (A)	ivory needles	$C_{14}H_{16}N_2O_2S_2$	54.52	5.23		9.08	20.79
			88 (D)	68.5-69.5° [c]		54.41	5.15		8.92	20.67
2i	4-*t*-BuC_6H_4	C_2H_5	83 (A)	yellowish-orange	$C_{17}H_{22}N_2O_2S_2$	58.25	6.33		7.99	18.30
				oil		58.41	6.43		8.31	18.20
2j	4-$CH_3OC_6H_4$	C_2H_5	60 (A)	ivory needles	$C_{14}H_{16}N_2O_3S_2$	51.83	4.97		8.63	19.77
				50.5-51.5° [d]		52.10	5.18		8.95	19.63
2k	3,4,5-$(CH_3O)_3C_6H_2$	C_2H_5	35 (A)	ivory needles	$C_{16}H_{20}N_2O_5S_2$	49.98	5.24		7.29	16.68
				27.0-27.5° [e]		50.19	5.30		7.20	16.61
2l	2-naphthyl	C_2H_5	38 (A)	ivory crystals	$C_{17}H_{16}N_2O_2S_2$	59.28	4.68		8.13	18.62
				46.5-47.5° [e]		59.59	4.97		8.07	18.89
2m	2-thienyl	C_2H_5	45 (A)	light orange oil	$C_{11}H_{12}N_2O_2S_3$	43.98	4.03		9.32	32.02
						44.05	3.99		9.24	31.98
2n	4-ClC_6H_4	C_2H_5	65 (A)	ivory cubes	$C_{13}H_{13}ClN_2O_2S_2$	47.48	3.98	10.78	8.52	19.50
				71.5-73.5° [d]		47.77	4.23	10.69	8.26	19.62
2o	4-FC_6H_4	C_2H_5	75 (A)	ivory needles	$C_{13}H_{13}FN_2O_2S_2$	49.98	4.19	6.08	8.97	20.53
				76.5-77.5° [d]		49.62	4.21	6.06	8.91	20.78
2p	3-$CH_3OC_6H_4$	C_2H_5	82 (A)	light orange oil	$C_{14}H_{16}N_2O_3S_2$	51.83	4.97		8.63	19.77
						52.00	4.97		8.45	19.56
2q	3-$CF_3C_6H_4$	CH_3	45 (A)	light orange oil	$C_{13}H_{11}F_3N_2O_2S_2$	44.82	3.18	16.36	8.04	18.42
						44.75	3.00	16.45	8.00	18.48
2r	$C_6H_5CH_2$	CH_3	60 (B)	light orange oil	$C_{13}H_{14}N_2O_2S_2$	53.04	4.79		9.51	21.78
						52.95	4.75		9.61	21.85
2s	C_6H_5S	C_2H_5	65 (A)	light orange oil	$C_{13}H_{14}N_2O_2S_3$	47.83	4.32		8.58	29.47
						47.75	4.25		8.35	29.55
2t	2-tetrahydropyranyl	CH_3	40 (A)	light yellow oil	$C_{11}H_{16}N_2O_3S_2$	45.82	5.59		9.71	22.24
						45.75	5.45		9.65	22.03

[a] A = Cyclization of thiocarbazonate ester; B = Cyclization of thiosemicarbazonate ester; C = Cyclization of *p*-tosylthiohydrazonate ester; D = Alkylation of thiolate salt. [b] Cyclization done in refluxing chloroform. [c] Methylcyclohexane. [d] Diisopropyl ether. [d] Diethyl ether (-40°).

As expected, treatment of **11-13** with thionyl chloride (*ca.* 2 equivalents) in chlorinated solvents afforded the 1,2,3-thiadiazoles **2-3** in moderate to excellent yields (Scheme I). In contrast to the crystalline 1,2,3-thiadiazoles, some of the oily 1,2,3-thiadiazoles (*e.g.* **2a-d,3a,3l**) discolored on exposure to direct light; however, for further synthetic studies this was of no major consequence (Table III and IV). Deprotection of the 4-(3-alkoxycarbonylethylthio)-1,2,3-thiadiazoles **2** with sodium (or potassium) ethoxide occurred smoothly to yield the desired thiolates **1** in >75% yields. Alternatively, the 4-methylthio-1,2,3-thiadiazoles (**3**, R = aryl; R' = CH_3) could be converted to the thiolates **1** *via* a modified Plummerer rearrangement of the corresponding sulfoxides **15**, albeit in inferior yields. With the exception of the parent thiolate **1a**, the thiolates were stable to nonacidic organic solvents for spectroscopic studies and chemical transformations. The infrared spectra of the thiolates **1** (potassium or sodium), in potassium

Table IV

Physical Constants of 4-(Alkylthio)(or Arylthio)-1,2,3-thiadiazoles **3**



Compound	R	R'	Yield, % [a]	Mp, °C	Formula	Analysis (Calcd./Found) C	H	Cl(F)	N	S
3a	H	C_2H_5	45 (A)	light yellow oil	$C_4H_6N_2S_2$	32.86	4.14		19.15	43.86
						32.56	3.89		18.97	44.03
3b	$(CH_3)_3C$	C_6H_5	75 (A)	yellow oil	$C_{12}H_{14}N_2S_2$	57.56	5.64		11.19	25.61
						57.97	5.61		11.43	25.51
3c	C_6H_5	C_6H_5	65 (A)	yellow oil	$C_{14}H_{10}N_2S_2$	62.19	3.73		10.36	23.72
						62.33	3.83		10.13	23.42
3d	$C_2H_5O_2C$	CH_3	45 (A)	ivory cubes	$C_6H_8N_2O_2$	35.28	3.95		13.71	31.39
				64.5-65.5° [b]		34.99	3.87		13.60	31.70
3e	2-thienyl	CH_3	75 (A)	yellow platelets	$C_7H_6N_2S_3$	39.23	2.82		13.07	44.88
				49.0-49.5° [c]		39.54	2.80		13.20	44.64
3f	4-$CH_3OC_6H_4$	CH_3	82 (A)	off-white needles	$C_{10}H_{10}N_2OS_2$	50.40	4.23		11.75	26.91
				60.5-61.0° [d]		50.45	4.01		11.77	26.81
3g	3-$CF_3C_6H_4$	CH_3	92 (B)	light orange oil	$C_{10}H_7F_3N_2S_2$	43.47	2.55	20.63	10.14	23.21
						43.67	2.79	20.40	10.16	22.98
3h	4-$CH_3C_6H_4$	$C_2H_5O_2CCH_2$	75 (A)	ivory cubes	$C_{13}H_{14}N_2O_2S_2$	53.04	4.79		9.52	21.78
			85 (B)	60.0-60.5° [e]		53.39	5.05		9.55	22.06
3i	4-*t*-BuC_6H_4	C_2H_5	55 (A)	yellow oil	$C_{14}H_{18}N_2S_2$	60.39	6.52		10.06	23.03
			95 (B)			60.61	6.66		10.14	22.77
3j	4-*t*-BuC_6H_4	$CH_2=CHCH_2$	90 (B)	yellow oil	$C_{15}H_{18}N_2S_2$	62.03	6.25		9.64	22.08
						61.95	6.12		9.55	21.95
3k	4-*t*-BuC_6H_4	$C_2H_5O_2CH_2$	78 (A)	white needles	$C_{16}H_{20}N_2O_2S_2$	57.12	5.99		8.32	19.06
			92 (B)	62.5-63.5° [f]		57.32	6.03		8.24	18.97
3l	$C_6H_5CH_2$	$C_2H_5O_2CC(CH_3)_2$	78 (B)	light orange oil	$C_{15}H_{18}N_2O_2S_2$	55.88	5.63		8.68	19.89
						55.73	5.46		8.35	19.74
3m	C_6H_5	$NCCH_2CH_2$	66 (A)	ivory crystals	$C_{11}H_9N_3S_2$	53.42	3.67		16.99	25.93
				63.5-64.5° [f]		53.30	3.60		17.00	25.95

[a] A = Cyclization of thiocarbazonate ester; B = Alkylation of thiolate salt. [b] Diisopropyl ether. [c] Diisopropyl ether-heptane. [d] *t*-butyl methyl ether. [d] Diethyl ether-petroleum ether (80-105°). [f] Methylcyclohexane.

Table V

Spectroscopic Properties of 1,2,3-Thiadiazoles **2-3**

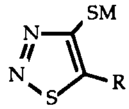
Compound	^{1}H NMR (δ [ppm], deuteriochloroform [a]	IR (ν [cm^{-1}])
2a	2.76 (t, 2H, *J* = 6.5 Hz, CH_2CO_2), 3.48 (t, 2H, SCH_2), 3.71 (s, 3H, OCH_3), 8.33 (s, 1H, H-5)	
2b	1.28 (t, 3H, *J* = 7.0 Hz, CH_3), 2.79 (t, 2H, *J* = 6.5 Hz, CH_2CO_2), 3.48 (t, 2H, SCH_2), 416 (q, 2H, OCH_2), 8.35 (s, 1H, H-5)	[c] 3120 (m), 1740 (s), 1260-1125 (s), 946-885
2c	1.26 (t, 3H, *J* = 7.0 Hz, CH_3CH_2O), 2.55 (s, 3H, CH_3), 2.70 (t, 2H, *J* = 7.0 Hz, CH_2CO), 3.39 (t, 2H, SCH_2), 4.14 (q, 2H, OCH_2)	[c] 1735 (s), 1460 (w), 1420 (w), 1370 (m), 1342 (m), 1285 (m), 1245 (m), 1218 (m), 1170 (m), 1140 (m), 1045 (m), 1040 (m), 1025 (m), 1010 (m), 890 (m)
2d	1.27 (t, 3H, *J* = 7.2 Hz, CH_3CH_2O), 1.36 (t, 3H, *J* = 7.0 Hz, CH_3CH_2), 2.73 (t, 2H, CH_2CO), 2.96 (q, 2H, $CH_2C=$), 3.43 (t, 2H, SCH_2)	[c] 1735 (s), 1460 (w), 1415 (w), 1370 (m), 1342 (w), 1285 (w), 1245 (w), 1220 (m), 1170 (m), 1140 (m), 1045 (m), 1025 (m), 1010 (m), 890 (m)
2e	1.51 (s, 9H, *t*-butyl), 2.85 (t, 2H, *J* = 6.5 Hz, CH_2CO), 3.60 (t, 2H, SCH_2), 3.70 (s, 3H, OCH_3)	[c] 1735 (s), 1460 (m), 1430 (m), 1400 (m), 1355 (m), 1245 (m), 1210 (m), 1170 (m), 1150 (m), 925 (m)
2f	1.23 (t, 3H, *J* = 7.0 Hz, CH_3), 1.49 (s, 9H, *t*-butyl), 2.84 (t, 2H, *J* = 7.0 Hz, CH_2CO), 3.59 (t, 2H, SCH_2), 4.14 (q, 2H, OCH_2)	
2g	1.22 (t, 3H, *J* = 7.0 Hz, CH_3), 2.76 (t, 2H, *J* = 6.5 Hz, CH_2CO), 3.52 (t, 2H, SCH_2), 4.08 (q, 2H, OCH_2), 7.53 (bs, 5H, C_6H_5)	[d] 1740 (s), 1225 (s), 1195 (s), 1175 (s), 1155 (s), 1015 (s), 932 (s), 758 (s), 685-690 (s)
2h	1.22 (t, 3H, *J* = 7.0 Hz, CH_3), 2.42 (s, 3H, $CH_3C_6H_4$), 2.80 (t, 2H, *J* = 7.5 Hz, CH_2CO_2), 3.58 (t, 2H, SCH_2), 4.15 (q, 2H, OCH_2), [7.27 (d, 2H, *J* = 8.0 Hz) and 7.50 (d, 2H) (C_6H_4)]	[d] 1735 (s), 1518 (w), 1480 (w), 1460 (w), 1440 (w), 1412 (w), 1400 (w), 1365 (w), 1230 (m), 1200 (s), 1160 (m), 1021 (m), 935 (m), 820 (m)

2i	1.24 (t, 3H, J = 7.0 Hz, CH_3), 1.32 (s, 9H, t-butyl), 2.83 (t, 2H, J = 6.5 Hz, CH_2CO_2), 3.60 (t, 2H, SCH_2), 4.15 (q, 2H, OCH_2), 7.55 (s, 4H, C_6H_4)	[c] 1740 (s), 1610 (m), 1522 (m), 1375 (m), 1270 (m), 1250 (m), 1220 (m), 1200 (m), 1180 (m), 935 (s), 840 (s)
2j	1.21 (t, 3H, J = 7.0 Hz, CH_3), 2.78 (t, 2H, J = 7.0 Hz, CH_2CO_2), 3.51 (t, 2H, SCH_2), 3.85 (s, 3H, OCH_3), 4.12 (q, 2H, OCH_2), [6.99 (d, 2H, J = 9.0 Hz) and 7.55 (d, 2H) (C_6H_4)]	[d] 1735 (s), 1615 (m), 1520 (m), 1480 (w), 1465 (w), 1445 (w), 1418 (w), 1400 (w), 1370 (w), 1355 (w), 1265 (m), 1225 (m), 1205 (m), 1180 (m), 1155 (m), 1035 (m), 1018 (m), 835 (m)
2k	1.24 (t, 3H, J = 7.0 Hz, CH_3), 2.82 (t, 2H, J = 6.5 Hz, CH_2CO_2), 3.60 (t, 2H, SCH_2), 3.91 [s, 9H, OCH_3 (3 x)], 4.15 (q, 2H, OCH_2), 6.81 (s, 2H, C_6H_2)	[d] 1735 (s), 1580 (s), 1515 (s), 1470 (s), 1415 (s), 1330 (s), 1250 (s), 1240 (m), 1180 (m), 1130 (s)
2l	1.23 (t, 3H, J = 7.0 Hz, CH_3), 2.84 (t, 2H, J = 7.0 Hz, CH_2CO_2), 3.60 (t, 2H, SCH_2, 4.13 (q, 2H, OCH_2, 7.45-8.25 (m, 7H, H arom)	
2m	1.24 (t, 3H, J = 7.0 Hz, CH_3), 2.83 (t, 2H, J = 7.0 Hz, CH_2CO_2), 3.61 (t, 2H, SCH_2), 4.14 (q, 2H, OCH_2), [6.97 (dd, 1H) and 7.41 (m, 2H) (H arom)]	
2n	1.24 (t, 3H, J = 7.0 Hz, CH_3), 2.78 (t, 2H, J = 7.0 Hz, CH_2CO_2), 3.56 (t, 2H, SCH_2), 4.10 (q, 2H, OCH_2), 7.50 (A_2B_2 quartet, 4H, C_6H_4)	[d] 1725 (s), 1590 (w), 1500 (m), 1400 (w), 1370 (w), 1280 (w), 1250 (w), 1220 (m), 1175 (m), 1150 (m), 1090 (m), 1010 (m), 930 (m), 830 (m)
2o	1.23 (t, 3H, J = 7.0 Hz, CH_3), 2.80 (t, 2H, J = 7.0 Hz, CH_2CO_2), 3.56 (t, 2H, SCH_2), 4.13 (q, 2H, OCH_2), [7.20 (dd, 2H, $^3J_{H\text{-}F}$= 8.0 Hz, J = 8.0 Hz) and 7.61 (dd, 2H, $^4J_{H\text{-}F}$ = 5.5 Hz) (C_6H_4)]	[d] 1730 (s), 1605 (w), 1520 (m), 1475 (w), 1440 (w), 1410 (w), 1375 (w), 1355 (w), 1255 (w), 1240 (m), 1220 (m), 1200 (w), 1050 (w), 1020 (w), 930 (m), 830 (m)
2p	1.23 (t, 3H, J = 7.0 Hz, CH_3), 2.79 (t, 2H, J = 7.0 Hz, CH_2CO_2), 3.55 (t, 2H, SCH_2), 3.82 (s, 3H, OCH_3), 4.10 (q, 2H, OCH_2), 6.80-7.55 (m, 4H, C_6H_4)	[c] 1725 (s), 1590 (m), 1575 (m), 1458 (m), 1450 (m), 1420 (m), 1370 (m), 1345 (m), 1295 (m), 1280 (m), 1245 (m), 1185 (m), 1160 (m), 1051 (m), 936 (m), 860 (m), 780 (m)
2q	2.86 (t, 2H, J = 7.0 Hz, CH_2CO_2), 3.57 (t, 2H, SCH_2), 3.66 (s, 3H, OCH_3), 7.55-7.85 (m, 4H, C_6H_4)	
2r	2.85 (t, 2H, J = 7.0 Hz, CH_2CO_2), 3.57 (t, 2H, SCH_2), 3.65 (s, 3H, OCH_3), 4.31 (s, 2H, $CH_2C_6H_5$), 7.30 (m, 5H, C_6H_5)	[c] 1735 (s), 1495 (w), 1435 (m), 1355 (m), 1245 (s), 1220 (m), 1200 (m), 1170 (m), 705 (m)
2s	1.27 (t, 3H, J = 7.2 Hz, CH_3CH_2O), 2.79 (t, 2H, J = 7.0 Hz, CH_2CO_2), 3.44 (t, 2H, SCH_2), 4.17 (q, 2H, OCH_2), 7.40-7.70 (bs, 5H, C_6H_5	[c] 1735 (s), 1575 (m), 1475 (m), 1435 (m) 1385 (m), 1370 (m), 1345 (m), 1245 (s), 1210 (s), 1185 (s), 1150 (s), 1055 (m), 1020 (m), 930-925 (m), 750 (s), 690 (s)
2t	[b] 1.50-2.20 [m, 6H, $(CH_2)_3CH_2O$], 2.80 (t, 2H, J = 7.0 Hz, CH_2CO_2), 3.45-3.60 (m, 2H, CH_2O), 3.55 (t, 2H, SCH_2), 3.70 (s, 3H, CH_3O), 5.22 (dd, 1H, J = 7.8 Hz, 6.0 Hz, CHO)	[c] 1742 (s), 1440 (s), 1360 (s), 1295 (w), 1245 (m), 1220 (m), 1200 (m), 1170 (m), 1150 (m), 935 (m)
3a	1.38 (t, 3H, J = 7.0 Hz, CH_3), 3.17 (q, 2H, SCH_2), 8.25 (s, 1H, H-5)	[c] 3120 (m), 1415 (s), 1265-1245 (s), 1210 (s), 950 (s), 884 (s), 820-720 (m)
3b	1.58 (s, 9H, t-butyl), 7.29 (bs, 5H, C_6H_5)	[c] 1585 (m), 1480 (s), 1442 (m), 1370 (m), 1250 (m), 1219 (m), 1180 (m), 1028 (w), 926 (s), 745 (m), 710 (s), 695 (s)
3c	7.28 (bs, 5H, C_6H_5), 7.30-7.65 (m, 5H, C_6H_5)	[c] 1580 (m), 1475 (s), 1440 (s), 1286 (w), 1265 (m), 1255 (m), 1240 (w), 1025 (w), 1005 (w), 985 (w), 935 (m), 915 (m), 805 (m), 765 (m), 745 (s), 695 (s)
3d	1.37 (t, 3H, J = 7.0 Hz, CH_3CH_2O), 2.87 (s, 3H, SCH_3), 4.39 (q, 2H, OCH_2)	[d] 1710 (s), 1470 (w), 1440 (w), 1430 (w), 1365 (w), 1320 (w), 1305 (s), 1175 (s), 1085 (s), 1085 (s), 1010 (m), 970 (m)
3e	2.85 (s, 3H, SCH_3), [6.96 (dd, 1H) and 7.41 (m, 2H) (C_4H_3S)]	[d] 1435 (m), 1420 (m), 1390 (s), 1352 (m), 1250 (s), 1220 (m), 1195 (m), 1160 (m), 920 (m), 705 (s)
3f	2.81 (s, 3H, SCH_3), 3.86 (s, 3H, OCH_3), [7.02 (d, 2H, J = 9.0 Hz) and 7.57 (d, 2H, (C_6H_4)]	[d] 1605 (m), 1515 (m), 1460 (w), 1450 (w), 1435 (m), 1400 (m), 1300 (m), 1265 (m), 1245 (s), 1210 (w), 1175 (m), 1022 (s), 930 (m), 830 (s)
3g	2.85 (s, 3H, SCH_3), 7.45-8.00 (m, 4H, H arom)	[c] 1495 (w), 1465 (w), 1430 (w), 1415 (w), 1325 (s), 1250 (s), 1170 (s), 1125 (s), 1070 (m), 1005 (w), 935 (m), 895 (m), 800 (m), 695 (m)
3h	1.21 (t, 3H, J = 7.0 Hz, CH_3), 2.42 (s, 3H, CH_3), 4.10 (s, 2H, SCH_2), 4.17 (q, 2H, OCH_2), [7.32 (d, 2H, J = 8.0 Hz) and 7.55 (d, 2H) (C_6H_4)]	[d] 1736 (s), 1515 (w), 1475 (w), 1440 (w), 1400 (w), 1380 (w), 1370 (w), 1315 (s), 1290 (w), 1250 (w), 1225 (w), 1175 (s), 1168 (s), 1025 (m), 930 (m), 815 (m)
3i	1.37 (s, 9H, t-butyl), 1.39 (t, 3H, J = 7.0 Hz, CH_3), 3.35 (q, 2H, SCH_2), 7.54 (s, 4H, C_6H_4)	[c] 1610 (w), 1520 (w), 1475 (w), 1460 (w), 1445 (w), 1405 (w), 1365 (w), 1270 (s), 1175 (s), 936 (s), 820 (s)
3j	1.39 (s, 9H, t-butyl), 3.98 (bd, 2H, SCH_2), 5.05 (bd, 1H, CH=), 5.20 (bd, 1H, CH=), 5.87 (m, 1H, CH_2CH=), 7.55 (s, 4H, C_6H_4)	[c] 1640 (w), 1615 (w), 1525 (w), 1480 (w), 1475 (w), 1450 (w), 1410 (w), 1370 (w), 1270 (w), 930 (s), 820 (s)
3k	1.21 (t, 3H, J = 7.0 Hz, CH_3), 1.37 (s, 9H, t-butyl), 4.11 (s, 2H, SCH_2), 4.15 (q, 2H, OCH_2), 7.55 (s, 4H, C_6H_4)	[d] 1739 (s), 1606 (w), 1520 (w), 1480 (w), 1445 (w), 1385 (w), 1365 (w), 1305 (s), 1175 (s), 1040 (w), 935 (s), 840 (s)
3l	1.22 (t, 3H, J = 7.0 Hz, CH_3CH_2), 1.67 [s, 6H, CH_3 (2x)], 4.12 (q, 2H, OCH_2CH_3), 4.31 (s, 2H, $CH_2C_6H_5$), 7.30 (bs, 5H, C_6H_5)	[c] 1735 (s), 1495 (w), 1435 (m), 1355 (m), 1245 (s), 1220 (s), 1200 (m), 1170 (m)
3m	2.90 (t, 2H, J = 6.5 Hz, CH_2CN), 3.55 (t, 2H, SCH_2), 7.54 (m, 5H, C_6H_5)	[d] 2250 (m), 1430 (s), 1325 (m), 1295 (m), 1260 (s), 1215 (m), 1185 (s), 935 (s), 765 (s), 695 (s)

[a] 90 MHz. [b] 300 MHz. [c] Film. [d] Potassium bromide pellet.

Table VI

Physical Constants of 1,2,3-Thiadiazole-4-thiolates **1**



Compound	R	M	¹H NMR (δ [ppm], perdeuteriomethanol) (90 MHz)	IR (ν [cm⁻¹]) (potassium bromide)	Formula	Analysis (Calcd./Found) C	H	N	S
1a	H	K	7.86 (s, 1H, H-5)		$C_2HKN_2S_2$				
1b	CH_3	Na	2.53 (s, 3H, CH_3)	1620 (m), 1580 (m), 1420 (s), 1375 (w), 1240 (s), 1200 (s), 1190 (m), 1125 (m), 1061 (s), 1000 (m), 895 (s)	$C_3H_3NaN_2S_2$				
1c	C_2H_5	Na	1.31 (t, 3H, J = 6.8 Hz, CH_3), 2.93 (q, 2H, CH_2)	1615 (m), 1580 (m), 1455 (m), 1415 (s), 1380 (m), 1240 (m), 1185 (s), 1135 (m)	$C_4H_5NaN_2S_2$ ·0.25 H_2O	27.82 27.65	3.21 2.99	16.22 16.06	37.13 37.41
1d	$(CH_3)_3C$	Na	1.55 (s, 9H, *t*-butyl)	1605 (w), 1450-1465, 1365 (s), 1255 (m), 1158 (m), 928 (s)	$C_6H_9NaN_2S_2$ ·0.5 H_2O	35.11 34.89	4.91 5.08	13.65 13.44	31.24 31.55
1e	C_6H_5	K	[7.40 (m, 1H), 7.45 (m, 2H) and 8.06 (m, 2H) (C_6H_5)]	1598 (w), 1499 (w), 1405 (w), 1262 (m), 1195 (s), 1127 (m), 930-940, 760 (s), 680-700 (s)	$C_7H_5KN_2S_2$ ·0.33 H_2O	40.31 40.48	2.40 2.19	11.75 11.39	26.90 26.59
1f	4-$CH_3C_6H_4$	K	2.35 (s, 3H, CH_3), [7.24 (d, 2H, J = 8.5 Hz) and 8.05 (d, 2H) (C_6H_4)]	1605 (w), 1520 (m), 1400 (s), 1265 (m), 1195 (s), 1135 (m), 930 (m), 835 (s), 810 (s)	$C_9H_7KN_2S_2$ ·0.1 H_2O	43.56 43.66	2.92 2.99	11.29 11.03	25.84 26.02
1g	4-*t*-BuC_6H_4	K	1.35 (s, 9H, *t*-butyl), [7.42 (d, 2H, J = 8.5 Hz) and 8.12 (d, 2H) (C_6H_4)]	1605 (w), 1520 (m), 1465 (m), 1400 (s), 1245-1270, 1170 (s), 1130 (m), 929 (s), 820 (s)	$C_{12}H_{13}KN_2S_2$ ·0.5H_2O	48.45 48.61	4.74 4.49	9.42 9.21	21.55 21.29
1h	3-$CF_3C_6H_4$	Na	[7.55 (m, 2H), 8.20 (m, 1H) and 8.75 (m, 1H) (H arom)]	1605 (w), 1442 (m), 1375 (m), 1300-1320, 1240 (m), 1165-1180 (s), 1110-1130 (m), 1065 (m), 1002 (m), 920 (s), 878 (s), 794 (s), 687 (s)	$C_9H_4F_3NaN_2S_2$ ·0.2 H_2O	37.55 37.26	1.54 1.31	9.73 9.59	22.28 22.35

bromide, showed intense characteristic absorptions in the range of 1360-1450 cm⁻¹ and 1150-1200 cm⁻¹ and a weaker absorption at 1595-1610 cm⁻¹ (Table VI). As expected, the thiolates **1** underwent reactions smoothly with various alkylating agents; however attempts to isolate the free thiols by careful acidification led to decomposition products.

At the planning stage, it was clear that shorter alternative syntheses of the desired 1,2,3-thiadiazoles **1-3** could be devised, provided that the thiocarbazonate esters **11** underwent cyclization. With the realization of this transformation, we then focussed attention on the development of a more efficient sequence to esters **11-13**. The reaction of hydrazonoyl chlorides (carbazidic chlorides, **20**) and *p*-toluenesulfonylhydrazonoyl chlorides **21** with mercaptans was then investigated [24,25]. The halides **20-21** were readily obtained from the corresponding N^2-acylcarbazates **16** or N^2-acyl-N^1-(*p*-toluenesulfonyl)hydrazides **17** on treatment with either phosphorus pentachloride or triphenylphosphine dichloride. Direct chlorination (chlorine or *t*-butyl hypochlorite) of carbazones **18** or arenesulfonylhydrazones **19** also provided a satisfactory entry to the halides **20-21**. However, this process was not amenable to substituents prone to electrophilic chlorination (*e.g.* R = 3,4,5-trimethoxyphenyl). Subsequent treatment of **20-21** with various thiols, in the presence of base, then afforded esters **11** (or **13**) in moderate yields with the *Z*(syn)-isomers predominating. This complementary sequence thus allows access to esters **11** (or **13**) not available by *S*-alkylation of either **8** or **10** (*e.g.* R′ = C_6H_5).

Alternatively, 4-halogeno-1,2,3-thiadiazoles **22**, on treatment with sodium sulfide, could possibly yield the desired thiolates **1**. This approach could also provide data concerning the relative reactivity of 4-chloro-1,2,3-thiadiazoles **22** *vs.* the isomeric 5-chloro-1,2,3-thiadiazoles **23** [26]. With this in consideration, attempts to cyclize several halides **20-21** with thionyl chloride to the desired **22** were studied, but none were successful.

Scheme II

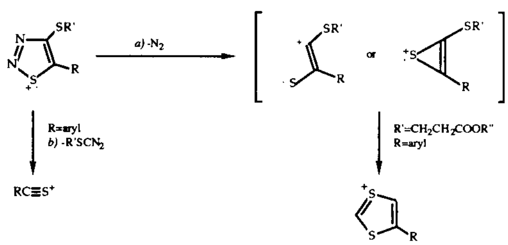


Table VII

Mass Spectra of 1,2,3-Thiadiazoles **2-3**

Compound	Mass Spectrum (EI), m/e (Relative Intensity)				
	$[M]^+$	$[M-28 (N_2)]^+$	$[R-C_3H_2S_2]^+$ [a]	$[R-C=S]^+$	Other Major Ions
2a	204 (3)	176 (25)	-	-	
2b	218 (2)	190 (22)	-	-	
2c	232 (4)	204 (22)	117 (28)	59 (100)	103 (40)
2d	246 (5)	218 (25)	131 (29)	73 (100)	103 (43)
2e	260 (20)	232 (30)	-	-	176 (40), 116 (42), 87 (46), 57 (100)
2g	294 (4)	266 (33)	179 (72)	121 (100)	
2h	308 (5)	280 (21)	193 (52)	135 (100)	
2i	350 (2)	322 (20)	235 (66)	177 (65)	221 (33), 147 (100)
2j	324 (10)	296 (30)	209 (60)	151 (100)	
2k	384 (10)	356 (33)	269 (43)	211 (100)	
2l	344 (2)	316 (44)	229 (80)	171 (100)	184 (35)
2m	300 (4)	272 (34)	185 (69)	127 (100)	
2n	330 (1)	302 (10)	215 (20)	157 (38)	
	328 (3)	300 (30)	213 (50)	155 (100)	
2o	312 (3)	284 (33)	197 (70)	139 (100)	
2p	324 (9)	296 (32)	209 (64)	151 (100)	
2q	348 (5)	320 (30)	247 (65)	189 (100)	
2r	294 (8)	266 (35)	193 (50)	135 (100)	
3b	250 (50)	222 (60)	-	-	166 (95), 121 (66), 57 (100)
3c	270 (25)	242 (40)	-	121 (100)	
3d	204 (40)	176 (20)	-	-	104 (75), 103 (100), 89 (46), 88 (100)
3e	214 (30)	186 (50)	-	127 (100)	139 (35)
3f	238 (20)	210 (55)	-	151 (100)	
3g	276 (10)	248 (32)	-	189 (100)	
3h	294 (5)	266 (29)	-	135 (100)	
3i	278 (10)	250 (30)	235 (100)	177 (70)	162 (40), 161 (30), 147 (55)
3j	290 (18)	-	-	177 (100)	162 (40), 147 (55)
3k	336 (60)	308 (40)	-	177 (100)	293 (38), 162 (48), 147 (52)
3m	247 (2)	219 (15)	179 (10)	121 (100)	

[a] 1,3-Dithiolium ion.

Table VIII

Table of Bond Angles in Degrees for **11Ef**

Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle
C3	S1	C4	102.9(1)	C4	C5	C6	114.9(2)	C12	C13	C16	123.1(2)
C1	O1	C2	116.2(2)	O3	C6	O4	122.6(3)	C14	C13	C16	120.7(2)
C6	O4	C7	118.9(3)	O3	C6	C5	125.1(3)	C13	C14	C15	122.0(2)
N2	N1	C2	121.0(2)	O4	C6	C5	112.2(2)	C10	C15	C14	121.3(2)
N1	N2	C3	117.0(2)	O4	C7	C8	110.1(3)	C13	C16	C17	109.7(2)
O1	C2	O2	124.0(2)	C3	C9	C10	112.1(2)	C13	C16	C18	109.6(2)
O1	C2	N1	113.0(2)	C9	C10	C11	120.8(2)	C13	C16	C19	112.0(2)
O2	C2	N1	123.0(2)	C9	C10	C15	121.8(2)	C17	C16	C18	108.4(3)
S1	C3	N2	119.3(2)	C11	C10	C15	117.4(2)	C17	C16	C19	107.2(3)
S1	C3	C9	113.1(1)	C10	C11	C12	121.1(2)	C18	C16	C19	109.9(3)
N2	C3	C9	127.6(2)	C11	C12	C13	122.0(2)				
S1	C4	C5	112.4(2)	C12	C13	C14	116.1(2)				

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

The mass spectra (ei) of the new 1,2,3-thiadiazoles **2-3** showed a characteristic $[M-28]^+$ ion arising from the loss of nitrogen [3b]; in addition, a prevalent ion observed for various 5-substituted-1,2,3-thiadiazoles was the $[R-C=S]^+$ ion. With the 4-(3-alkoxycarbonylethylthio)-5-aryl-1,2,3-thiadiazoles **2**, an additional characteristic 4-aryl-1,3-dithiolium ion was also observed (Scheme II and Table VII).

Table IX

Table of Bond Distances in Angstroms for **11Ef**

Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance
S1	C3	1.749(2)	N1	C2	1.341(3)	C11	C12	1.382(3)
S1	C4	1.800(2)	N2	C3	1.270(2)	C12	C13	1.373(3)
O1	C1	1.426(3)	C3	C9	1.506(3)	C13	C14	1.384(3)
O1	C2	1.332(2)	C4	C5	1.497(3)	C13	C16	1.537(3)
O2	C2	1.207(2)	C5	C6	1.469(3)	C14	C15	1.373(3)
O3	C6	1.198(3)	C7	C8	1.382(5)	C16	C17	1.507(3)
O4	C6	1.321(3)	C9	C10	1.526(3)	C16	C18	1.511(4)
O4	C7	1.449(4)	C10	C11	1.371(3)	C16	C19	1.522(4)
N1	N2	1.389(2)	C10	C15	1.371(3)			

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

Table X

Table of Bond Angles in Degrees for **11Zu**

Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle
C3	S1	C11	101.8(1)	C3	C4	H6	105.0(7)	C5	C10	H11	118.0(2)
C1	O2	C2	114.9(2)	C5	C4	H5	111.0(2)	C9	C10	H11	122.0(2)
N2	N1	C2	115.8(2)	C5	C4	H6	111.0(2)	S1	C11	C12	122.6(3)
N2	N1	H1	120.0(2)	H5	C4	H6	112.0(3)	S1	C11	C16	118.5(3)
C2	N1	H1	122.0(2)	C4	C5	C6	120.3(3)	C12	C11	C16	118.7(3)
N1	N2	C3	119.9(2)	C4	C5	C10	122.1(3)	C11	C12	C13	120.4(4)
O2	C1	H2	115.0(2)	C6	C5	C10	117.6(3)	C11	C12	H12	116.0(2)
O2	C1	H3	108.0(2)	C5	C6	C7	121.8(4)	C13	C12	H12	123.0(2)
O2	C1	H4	111.0(3)	C5	C6	H7	119.0(2)	C12	C13	C14	120.3(5)
H2	C1	H3	108.0(3)	C7	C6	H7	119.0(2)	C12	C13	H13	121.0(3)
H2	C1	H4	102.0(3)	C6	C7	C8	120.2(4)	C14	C13	H13	119.0(3)
H3	C1	H4	111.0(3)	C6	C7	H8	122.0(3)	C13	C14	C15	119.6(4)
O1	C2	O2	125.0(2)	C8	C7	H8	117.0(3)	C13	C14	H14	120.0(2)
01	C2	N1	125.0(2)	C7	C8	C9	119.1(4)	C15	C14	H14	120.0(2)
O2	C2	N1	110.0(2)	C7	C8	H9	117.0(2)	C14	C15	C16	120.8(4)
S1	C3	N2	123.6(2)	C9	C8	H9	124.0(2)	C14	C15	H15	121.0(3)
S1	C3	C4	119.3(2)	C8	C9	C10	121.1(4)	C16	C15	H15	118.0(3)
N2	C3	C4	116.9(3)	C8	C9	H10	120.0(2)	C11	C15	C15	120.2(4)
C3	C4	C5	112.2(2)	C10	C9	H10	119.0(2)	C11	C16	H16	116.0(2)
C3	C4	H5	106.0(2)	C5	C10	C9	120.1(3)	C15	C16	H16	123.0(2)

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

Table XI

Table of Bond Distances in Angstroms for **11Zu**

Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance
S1	C3	1.782(3)	C4	C5	1.508(4)	C10	H11	1.01(4)
S1	C11	1.753(3)	C4	H5	0.90(3)	C11	C12	1.366(4)
O1	C2	1.194(3)	C4	H6	0.80(3)	C11	C16	1.375(4)
O2	C1	1.441(3)	C5	C6	1.375(4)	C12	C13	1.374(6)
O2	C2	1.331(3)	C5	C10	1.380(4)	C12	H12	0.93(3)
N1	N2	1.371(3)	C6	C7	1.369(5)	C13	C14	1.363(6)
N1	C2	1.359(3)	C6	H7	0.91(3)	C13	H13	0.89(4)
N1	H1	0.83(3)	C7	C8	1.357(5)	C14	C15	1.348(6)
N2	C3	1.273(3)	C7	H8	0.92(4)	C14	H14	0.94(4)
C1	H2	1.02(4)	C8	C9	1.363(5)	C15	C16	1.371(5)
C1	H3	0.89(3)	C8	H9	0.99(3)	C15	H15	0.90(4)
Cl	H4	0.94(4)	C9	C10	1.379(5)	C16	H16	0.94(3)
C3	C4	1.521(4)	C9	H10	0.89(4)			

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

In conclusion, the cyclization of *N*-acylthiohydrazonate esters **11-13** with thionyl chloride provides a facile entry into derivatives of 1,2,3-thiadiazole-4-thiolates **1**. More importantly, as shown by the synthesis of **2s**, 4,5-biheteroatom functionalized 1,2,3-thiadiazoles may be attainable with the Hurd-Mori synthesis. New chemotherapeutic agents incorporating **1** will be the subject of further communications from these laboratories.

EXPERIMENTAL

Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. All column chromatographic purifications were accomplished on silica gel 60 (E. Merck, 230-400 mesh) or neutral alumina (Aldrich, 70-230 mesh) with the appropriate solvent gradients. Thin-layer chromatography was done on commercial silica gel plates (Analtech) containing calcium sulfate binder and fluorescent indicator. Melting points were determined in open Pyrex capillary tubes on a Meltemp melting point apparatus and are uncorrected. The ir spectra were recorded with either a Perkin-Elmer Model 1310 or a Nicolet Model 7199 recording infrared spectrophotometer. The ^{1}H nmr spectra were determined with either a Varian EM-390 (90 MHz) or Nicolet NT-300WB (300 MHz) spectrometer in appropriate deuterated solvents and are expressed in parts per million (δ, ppm) downfield from tetramethylsilane (internal standard). Significant ^{1}H nmr data are tabulated in order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; br, broad), number of protons, coupling constant(s) in Hz, and assignments. Mass spectra (ms) were obtained on a Varian CH7 mass spectrometer in electron impact mode (ei).

General Procedure for the Preparation of *N*-Thioacylpiperidides (4).

All of these reactions were carried out under an argon atmosphere. A suspension of the *N*-acylpiperidide and bis(4-methoxyphenyl)-1,3,2,4-dithiaphosphetane-2,4-disulfide (0.5 equivalents) in dry toluene (800 ml/mole of *N*-acylpiperidide) was heated, at reflux, for 6-8 hours. On cooling, the toluene solution was applied to a column of neutral alumina and eluted with methylene chloride. The eluate was concentrated *in vacuo* and the crude **4** was distilled or recrystallized from an appropriate solvent, as described [(a) all yields were >80%; (b) all unassigned ^{1}H nmr resonances are on the piperidine moiety].

N-(1-Thioxoethyl)piperidine (**4a**).

This compound was obtained as faint yellow crystals (toluene), mp 46.5-48.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.65-1.78 (m, 6H), 2.67 (s, 3H, CH_3), 3.60 (m, 2H), 4.25 (m, 2H).

Anal. Calcd. for $C_7H_{13}NS$: C, 58.69; H, 9.15; N, 9.77; S, 22.38. Found: C, 58.75; H, 9.10; N, 9.72; S, 22.46.

N-(1-Thioxopropyl)piperidine (**4b**).

This compound was obtained as a faint yellow liquid, bp 109.0-110.0°/2.0 mm Hg; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.25 (t, 3H, CH_3), 1.60-1.75 (m, 6H), 2.80 (q, 2H, CH_3CH_2), 3.60 (m, 2H), 4.21 (m, 2H).

Anal. Calcd. for $C_8H_{15}NS$: C, 61.10; H, 9.61; N, 8.90; S, 20.39. Found: C, 61.05; H, 9.72; N, 9.00; S, 20.25.

N-(1-Thioxobutyl)piperidine (**4c**).

This compound was obtained as a faint yellow liquid, bp 106.5-108.0°/0.5 mm Hg; ^{1}H nmr (90 MHz, deuteriochloroform): δ 0.98 (t, 3H, CH_3), 1.62-1.73 (m, 6H), 1.75 (m, 2H, CH_3CH_2), 2.75 (t, 2H, CH_2CS), 3.60 (m, 2H), 4.21 (m, 2H).

Anal. Calcd. for $C_9H_{17}NS$: C, 63.10; H, 10.00; N, 8.17; S, 18.72. Found: C, 63.05; H, 9.89; N, 8.25; S, 19.01.

N-(3,3-Dimethyl-1-thioxobutyl)piperidine (**4d**).

This compound was obtained as white platelets [petroleum ether (65-95°)], mp 59.5-60.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.10 (s, 9H, *t*-butyl), 1.70 (m, 6H), 2.96 (s, 2H, CH_2CS), 3.72 (m, 2H), 4.30 (m, 2H).

Anal. Calcd. for $C_{11}H_{21}NS$: C, 66.27; H, 10.62; N, 7.03; S, 16.08. Found: C, 66.54; H, 10.71; N, 6.68; S, 16.07.

N-(2-Phenyl-1-thioxoethyl)piperidine (**4e**).

This compound was obtained as yellow crystals (methylcyclohexane), mp 78.5-79.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.32 (m, 2H), 1.67 (m, 4H), 3.60 (m, 2H), 4.29 (m, 2H), 4.37 (s, 2H, CH_2CS), 7.32 (bs, 5H, C_6H_5).

Anal. Calcd. for $C_{13}H_{17}NS$: C, 71.19; H, 7.81; N, 6.39; S, 14.62. Found: C, 71.44; H, 7.56; N, 6.27; S, 14.59.

N-[2-(4-Methylphenyl)-1-thioxoethyl]piperidine (**4f**).

This compound was obtained as ivory crystals (toluene), mp 117.0-117.5°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.33 (m, 2H), 1.66 (m, 4H), 2.32 (s, 3H, CH_3), 3.61 (m, 2H), 4.30 (m, 2H), 4.33 (s, 2H, CH_2CS), 7.29 (A_2B_2 quartet, 4H, C_6H_4).

Anal. Calcd. for $C_{14}H_{19}NS$: C, 72.05; H, 8.21; N, 6.00; S, 13.74. Found: C, 71.72; H, 8.06; N, 5.80; S, 13.95.

N-[2-(4-*t*-Butylphenyl)-1-thioxoethyl]piperidine (**4g**).

This compound was obtained as ivory crystals (hexane), mp 104.0-105.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.31 (s, 9H, *t*-butyl), 1.35 (m, 2H), 1.68 (m, 4H), 3.61 (m, 2H), 4.29 (m, 2H), 4.31 (s, 2H, CH_2CS), 7.30 (bs, 4H, C_6H_4).

Anal. Calcd. for $C_{17}H_{25}NS$: C, 74.13; H, 9.15; N, 5.08; S, 11.64. Found: C, 74.41; H, 8.91; N, 4.92; S, 11.82.

N-[2-(4-Methoxyphenyl)-1-thioxoethyl]piperidine (**4h**).

This compound was obtained as ivory crystals (toluene-methylcyclohexane), mp 74.5-75.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.33 (m, 2H), 1.63 (m, 4H), 3.61 (m, 2H), 3.79 (s, 3H, CH_3O), 4.27 (m, 2H), 4.27 (s, 2H, CH_2CS), [6.88 (d, 2H, J = 9.0 Hz) and 7.29 (d, 2H) (C_6H_4)].

Anal. Calcd. for $C_{14}H_{19}NOS$: C, 67.43; H, 7.68; N, 5.62; S, 12.86. Found: C, 67.57; H, 7.87; N, 5.63; S, 12.86.

N-[2-(3,4,5-Trimethoxyphenyl)-1-thioxoethyl]piperidine (**4i**).

This compound was obtained as ivory crystals (methylcyclohexane), mp 79.0-81.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.35 (m, 2H), 1.65 (m, 4H), 3.61 (m, 2H), 3.85 (s, 3H, CH_3O), 3.87 (s, 6H, CH_3O, x 2), 4.27 (m, 2H), 4.31 (s, 2H, CH_2CS), 6.60 (s, 2H, C_6H_2).

Anal. Calcd. for $C_{16}H_{23}NO_3S$: C, 62.11; H, 7.49; N, 4.53; S, 10.36. Found: C, 62.10; H, 7.54; N, 4.35; S, 10.25.

N-[2-(2-Naphthyl)-1-thioxoethyl]piperidine (**4j**).

This compound was obtained as light yellow crystals (methylcyclohexane), mp 89.0-91.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.25 (m, 2H), 1.65 (m, 4H), 3.61 (m, 2H), 4.34 (m, 2H), 4.56 (s, 2H, CH_2CS), 7.25-8.00 (m, 7H, $C_{10}H_7$).

Anal. Calcd. for $C_{17}H_{19}NS$: C, 75.79; H, 7.11; N, 5.20; S, 11.90. Found: C, 75.65; H, 6.99; N, 5.15; S, 11.75.

N-[2-(2-Thienyl)-1-thioxoethyl]piperidine (**4k**).

This compound was obtained as ivory crystals (toluene-cyclohexane), mp 51.5-52.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.37 (m, 2H), 1.65 (m, 4H), 3.64 (m, 2H), 4.27 (m, 2H), 4.48 (s, 2H, CH_2CS), [6.95 (m, 2H) and 7.20 (m, 1H) (C_4H_3S)].

Anal. Calcd. for $C_{11}H_{15}NS_2$: C, 58.62; H, 6.71; N, 6.21; S, 28.45. Found: C, 58.71; H, 6.56; N, 6.00; S, 28.47.

N-[2-(4-Chlorophenyl)-1-thioxoethyl]piperidine (**4l**).

This compound was obtained as ivory crystals (methylcyclohexane), mp 82.5-84.5°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.37 (m, 2H), 1.67 (m, 4H), 3.59 (m, 2H), 4.28 (s, 2H, CH_2CS), 4.29 (m, 2H), 7.30 (bs, 4H, C_6H_4).

Anal. Calcd. for $C_{13}H_{16}ClNS$: C, 61.52; H, 6.35; Cl, 13.97; N, 5.52. Found: C, 61.79; H, 6.43; Cl, 14.00; N, 5.35.

N-[2-(4-Fluorophenyl)-1-thioxoethyl]piperidine (**4m**).

This compound was obtained as ivory crystals (methylcyclohexane), mp 68.0-69.5°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.35 (m, 2H), 1.66 (m, 4H), 3.59 (m, 2H), 4.25 (m, 2H), 4.31 (s, 2H, CH_2CS), [7.02 (dd, 2H, $J = {}^3J_{H,F}$ = 8.5 Hz) and 7.35 (dd, 2H, J = 8.5 Hz; $^4J_{H,F}$ = 6.5 Hz) (C_6H_4)].

Anal. Calcd. for $C_{13}H_{16}FNS$: C, 65.79; H, 6.79; F, 8.00; N, 5.90; S, 13.51. Found: C, 65.71; H, 6.75; F, 8.10; N, 5.64; S, 13.61.

N-[2-(3-Methoxyphenyl)-1-thioxoethyl]piperidine (**4n**).

This compound was obtained as yellow crystals (methylcyclohexane), mp 53.0-55.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.36 (m, 2H), 1.72 (m, 4H), 3.63 (m, 2H), 3.87 (s, 3H, CH_3O), 4.31 (m, 2H), 4.37 (s, 2H, CH_2CS), [6.90 (m, 3H) and 7.27 (m, 1H) (C_6H_4)].

Anal. Calcd. for $C_{14}H_{19}NOS$: C, 67.43; H, 7.68; N, 5.62; S, 12.86. Found: C, 67.48; H, 7.79; N, 5.45; S, 12.75.

N-[2-[3-(Trifluoromethyl)phenyl]-1-thioxoethyl]piperidine (**4o**).

This compound was obtained as an orange liquid, bp 181.0-182.0°/3.0 mm Hg; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.37 (m, 2H), 1.70 (m, 4H), 3.59 (m, 2H), 4.31 (m, 2H), 4.39 (s, 2H, CH_2CS), 7.55 (m, 4H, C_6H_4).

Anal. Calcd. for $C_{14}H_{16}F_3NS$: C, 58.52; H, 5.61; F, 19.84; N, 4.87; S, 11.16. Found: C, 58.63; H, 5.62; F, 19.58; N, 4.94; S, 11.18.

N-(3-Phenyl-1-thioxopropyl)piperidine (**4p**).

This compound was obtained as yellow crystals (methylcyclohexane), mp 65.0-66.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.65 (m, 6H), 3.10 [bs, 4H, $(CH_2)_2CS$], 3.59 (m, 2H), 4.28 (m, 2H), 7.25 (bs, 5H, C_6H_5).

Anal. Calcd. for $C_{14}H_{19}NS$: C, 72.05; H, 8.21; N, 6.00; S, 13.74. Found: C, 72.11; H, 8.42; N, 6.04; S, 13.89.

N-[2-(Phenylthio)-1-thioxoethyl]piperidine (**4q**).

This compound was obtained as yellow crystals (cyclohexane), mp 84.5-85.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.72 (m, 6H), 3.69 (m, 2H), 4.24 (m, 2H), 4.30 (s, 2H, CH_2CS), 7.35-7.65 (m, 5H, C_6H_5).

Anal. Calcd. for $C_{13}H_{17}NS_2$: C, 62.11; H, 6.82; N, 5.57; S, 25.51. Found: C, 62.25; H, 6.79; N, 5.26; S, 25.24.

(±)-*N*-[2-(Tetrahydro-2*H*-pyran-2-yl)-1-thioxoethyl]piperidine (**4r**).

This compound was obtained as an orange liquid, bp 168.0-172.0°/2.0 mm Hg; ^{1}H nmr (300 MHz, deuteriochloroform): δ 1.20-1.90 [m, 12H, $NCH_2(CH_2)_3$ and $OCH_2(CH_2)_3$], [2.89 (dd, 1H, J_{gem} = 13.4 Hz, J = 4.2 Hz) and 3.13 (dd, 1H, J_{gem} = 13.4 Hz; J = 8.1 Hz) ($CHCH_2CS$)], 3.41 (m, 1H, $OCHCH_2$), 3.70-4.00 (m, 4H), 4.10-4.40 (m, 2H, OCH_2).

Anal. Calcd. for $C_{12}H_{21}NOS$: C, 63.39; H, 9.31; N, 6.16; S, 14.10. Found: C, 63.03; H, 9.12; N, 6.12; S, 13.81.

Ethyl 3-Thioxo-*N*-piperidinepropionate (**4s**).

This compound was obtained as an orange liquid, bp 146.0-148.0°/0.5 mm Hg; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.29 (t, 3H, CH_3), 1.69 (m, 6H), 3.65 (m, 2H), 4.01 (s, 2H, CH_2CS), 4.19 (q, 2H, OCH_2), 4.28 (m, 2H).

Anal. Calcd. for $C_{10}H_{17}NO_2S$: C, 55.78; H, 7.96; N, 6.51; S, 14.89. Found: C, 55.74; H, 7.95; N, 6.64; S, 15.15.

General Procedure for the Preparation of 1-[1-[(Carboxymethyl)thio]-alkylidene]piperidinium Bromides **5** (R″ = H) and 1-[1-[(Ethoxycarbonylmethyl)thio]alkylidene]piperidinium Bromides **6** (R″ = C_2H_5).

A mixture of the *N*-thioacylpiperidide **4** and anhydrous bromoacetic acid (1.05 equivalents) (or ethyl bromoacetate) in anhydrous benzene (7 ml/g *N*-thioacylpiperidide) was stirred at ambient temperature for 12 hours. The resultant hygroscopic crystalline salt **5** (or **6**) was collected, washed with anhydrous ether, and dried *in vacuo*. The crude material was then utilized in the subsequent sulfhydrolysis reaction without further purification.

General Procedure for the Preparation of *S*-Thioacylthioglycolate Esters **7**.

A suspension of salt **5** (or **6**) in absolute ethanol (5 ml/g salt) was treated with hydrogen sulfide (1.5 equivalents) at ambient temperature. The resulting mixture was stirred and heated at reflux for 6 hours and concentrated *in vacuo*. The semicrystalline residue was suspended in anhydrous ether and the crystalline piperidine hydrobromide was collected and washed with ether. The filtrate was concentrated *in vacuo* and the crude dithioester **7** was flash chromatographed over a short column of magnesium trisilicate with methylene chloride. Additional purification of **7** was accomplished by either distillation or crystallization from the appropriate solvent, as described [(a) all yields were >70%; (b) all unassigned ^{1}H nmr resonances are on the alkoxy unit (C_2H_5O or CH_3O)].

Ethyl [(1-Thioxoethyl)thio]acetate (**7a**).

This compound was obtained as an orange liquid, bp 84.0-88.0°/1.0 mm Hg; ir (film): 1739, 1290, 1260, 1210, 1155, 1095, 1025, 860 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.31 (t, 3H), 2.90 (s, 3H, CH_3CS_2), 4.10 (s, 2H, SCH_2CO_2), 4.24 (q, 2H).

Anal. Calcd. for $C_6H_{10}O_2S_2$: C, 40.43; H, 5.65; S, 35.97. Found: C, 40.72; H, 5.69; S, 35.86.

Ethyl [(1-Thioxopropyl)thio]acetate (**7b**).

This compound was obtained as an orange liquid, bp 93.0-95.0°/1.0 mm Hg; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.28 (t, 3H), 1.38 (t, 3H, J = 7.4 Hz, $CH_3CH_2CS_2$), 3.05 (q, 2H, CH_2CS_2), 4.08 (s, 2H, SCH_2CO_2), 4.18 (q, 2H).

Anal. Calcd. for $C_7H_{12}O_2S_2$: C, 43.72; H, 6.29; S, 33.35. Found: C, 43.51; H, 6.10; S, 33.50.

Ethyl [(1-Thioxobutyl)thio]acetate (**7c**).

This compound was obtained as an orange liquid, bp 100.0-103.0°/0.8 mm Hg; ir (film): 1730 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.01 [t, 3H, J = 7.0 Hz, $CH_3(CH_2)_2$], 1.27 (t, 3H), 1.85 (m, 2H, $CH_3CH_2CH_2$), 3.04 (t, 2H, J = 7.5 Hz, CH_2CS_2), 4.07 (s, 2H, SCH_2CO_2), 4.15 (q, 2H).

Anal. Calcd. for $C_8H_{14}O_2S_2$: C, 46.57; H, 6.84; S, 31.08. Found: C, 46.46; H, 6.70; S, 31.20.

Methyl [(3,3-Dimethyl-1-thioxobutyl)thio]acetate (**7d**).

This compound was obtained as a light yellow liquid, bp 82.0-84.5°/0.5 mm Hg; ir (film): 1735, 1470, 1435, 1360, 1285, 1250, 1215, 1190, 1155, 1135, 965, 840 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.09 (s, 9H, *t*-butyl), 3.10 (s, 2H, CH_2CS_2), 3.72 (s, 3H), 4.10 (s, 2H, CH_2CO_2).

Anal. Calcd. for $C_9H_{16}O_2S_2$: C, 49.06; H, 7.32; S, 29.10. Found: C, 49.00; H, 7.21; S, 28.95.

Ethyl [(2-Phenyl-1-thioxoethyl)thio]acetate (**7e**).

This compound was obtained as yellow platelets (methylcyclohexane), mp 43.5-45.5°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.27 (t, 3H), 4.08 (s, 2H, SCH_2CO_2), 4.21 (q, 2H), 4.36 (s, 2H, CH_2CS_2), 7.33 (bs, 5H, C_6H_5).

Anal. Calcd. for $C_{12}H_{14}O_2S_2$: C, 56.66; H, 5.55; S, 25.21. Found: C, 56.51; H, 5.46; S, 25.15.

Ethyl [[2-(4-Methylphenyl)-1-thioxoethyl]thio]acetate (**7f**).

This compound was obtained as yellow needles [petroleum ether (35-65°)], mp 41.5-42.0°; ir (potassium bromide): 1732, 1515, 1365, 1300, 1165 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.28 (t, 3H), 2.31 (s, 3H, $CH_3C_6H_4$), 4.07 (s, 2H, SCH_2CO_2), 4.20 (q, 2H), 4.37 (s, 2H, CH_2CS_2), 7.24 (A_2B_2 quartet, 4H, C_6H_4).

Anal. Calcd. for $C_{13}H_{16}O_2S_2$: C, 58.18; H, 6.01; S, 23.89. Found: C, 58.38; H, 6.00; S, 24.17.

Ethyl [[2-(4-*t*-Butylphenyl)-1-thioxoethyl]thio]acetate (**7g**).

This compound was obtained as a yellow liquid, bp 140.0-144.0/0.5 mm Hg; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.28 (t, 3H), 1.35 (s, 9H, *t*-butyl), 4.09 (s, 2H, SCH_2CO_2), 4.19 (q, 2H), 4.37 (s, 2H, CH_2CS_2), 7.33 (bs, 4H, C_6H_4).

Anal. Calcd. for $C_{16}H_{22}O_2S_2$: C, 61.90; H, 7.14; S, 20.65. Found: C, 61.82; H, 7.02; S, 20.51.

Ethyl [[2-(4-Methoxyphenyl)-1-thioxoethyl]thio]acetate (**7h**).

This compound was obtained as yellow platelets (methylcyclohexane), mp 41.5-42.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.29 (t, 3H), 3.76 (s, 3H, CH_3O), 4.03 (s, 2H, SCH_2CO_2), 4.20 (q, 2H), 4.25 (s, 2H, CH_2CS_2), [6.84 (d, 2H, J = 8.0 Hz) and 7.26 (d, 2H) (C_6H_4)].

Anal. Calcd. for $C_{13}H_{16}O_3S_2$: C, 54.90; H, 5.67; S, 22.55. Found: C, 54.82; H, 5.62; S, 22.35.

Ethyl [[2-(4-Chlorophenyl)-1-thioxoethyl]thio]acetate (**7i**).

This compound was obtained as yellow platelets (methylcyclohexane), mp 36.5-37.0°; ir (potassium bromide): 1735, 1490, 1375, 1300, 1170 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.25 (t, 3H), 4.06 (s, 2H, SCH_2CO_2), 4.17 (q, 2H), 4.29 (s, 2H, CH_2CS_2), 7.29 (s, 4H, C_6H_4).

Anal. Calcd. for $C_{12}H_{13}ClO_2S_2$: C, 49.90; H, 4.54; Cl, 12.28; S, 22.20. Found: C, 49.75; H, 4.62; Cl, 12.10; S, 22.07.

Ethyl [[2-(4-Fluorophenyl)-1-thioxoethyl]thio]acetate (**7j**).

This compound was obtained as yellow platelets (methylcyclohexane), mp 45.5-47.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.26 (t, 3H), 4.03 (s, 2H, SCH_2CO_2), 4.18 (q, 2H), 4.30 (s, 2H, CH_2CS_2), [7.00 (dd, 2H, J = $^3J_{H,F}$ = 9.0 Hz) and 7.34 (dd, 2H, $^4J_{H,F}$ = 5.5 Hz, J = 9.0 Hz) (C_6H_4)].

Anal. Calcd. for $C_{12}H_{13}FO_2S_2$: C, 52.92; H, 4.81; F, 6.98; S, 23.54. Found: C, 52.78; H, 4.85; F, 6.82; S, 23.25.

Ethyl [[2-(3-Methoxyphenyl)-1-thioxoethyl]thio]acetate (**7k**).

This compound was obtained as yellow platelets (methylcyclohexane), mp 29.0-31.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.27 (t, 3H), 3.86 (s, 3H, CH_3O), 4.07 (s, 2H, SCH_2CO_2), 4.16 (q, 2H), 4.35 (s, 2H, CH_2CS_2), [6.89 (m, 3H) and 7.29 (m, 1H) (C_6H_4)].

Anal. Calcd. for $C_{13}H_{16}O_3S$: C, 54.90; H, 5.67; S, 22.55. Found: C, 54.85; H, 5.55; S, 22.70.

Ethyl [[1-Thioxo-2-[3-(trifluoromethyl)phenyl]thio]acetate (**7l**).

This compound was obtained as a yellowish-orange liquid, bp 176.0-178.0°/5.0 mm Hg; ir (film): 1724, 1440, 1322, 1290, 1155, 1120 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.25 (t, 3H), 4.05 (s, 2H, SCH_2CO_2), 4.15 (q, 2H), 4.36 (s, 2H, CH_2CS_2), 7.50 (m, 4H, C_6H_4).

Anal. Calcd. for $C_{13}H_{13}F_3O_2S_2$: C, 48.44; H, 4.06; F, 17.68; S, 19.89. Found: C, 48.93; H, 4.23; F, 17.90; S, 19.69.

Ethyl [(3-Phenyl-1-thioxopropyl)thio]acetate (**7m**).

This compound was obtained as a light orange liquid, bp 180.0-183.0°/0.8 mm Hg; ir (film): 1735, 1295, 1155, 1025 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.28 (t, 3H), 3.00-3.45 [m, 4H, $(CH_2)_2$], 4.05 (s, 2H, SCH_2CO_2), 4.19 (q, 2H), 7.24 (bs, 5H, C_6H_5).

Anal. Calcd. for $C_{13}H_{16}O_2S_2$: C, 58.18; H, 6.01; S, 23.89. Found: C, 58.22; H, 5.87; S, 24.05.

Methyl [(2-Phenylthio-1-thioxoethyl)thio]acetate (**7n**).

This compound was obtained as an orange liquid which was used without further purification; ^{1}H nmr (90 MHz, deuteriochloroform): δ 3.68 (s, 3H), 4.00 (s, 2H, SCH_2CO_2), 4.31 (s, 2H, SCH_2CS_2), 7.36 (m, 5H, C_6H_5).

Anal. Calcd. for $C_{12}H_{14}O_2S_3$: C, 50.32; H, 4.93; S, 33.58. Found: C, 50.15; H, 5.02; S, 33.70.

(±) Ethyl [[2-(Tetrahydro-2*H*-pyran-2-yl)-1-thioxoethyl]thio]acetate (**7o**).

This compound was obtained as a yellow liquid which was used without further purification; ^{1}H nmr (300 MHz, deuteriochloroform): δ 1.27 (t, 3H), 1.25-1.90 [m, 6H, $OCH_2(CH_2)_3$], [3.03 (dd, 1H, J_{gem} = 13.7 Hz, J = 5.3 Hz) and 3.31 (dd, 1H, J_{gem} = 13.7 Hz; J = 7.6 Hz) ($CHCH_2CS_2$)], 3.42 (m, 1H, $OCHCH_2$), 3.85-4.00 (m, 2H, OCH_2), 4.06 (AB quartet, 2H, SCH_2CO_2), 4.19 (q, 2H).

Anal. Calcd. for $C_{11}H_{18}O_3S_2$: C, 50.35; H, 6.91; S, 24.44. Found: C, 50.13; H, 6.98; S, 24.47.

General Procedure for the Preparation of Methyl (or Ethyl) 2-[1-Thioxoalkyl]hydrazinocarboxylate **8** (N_2-Thioacylcarbazates).

A mixture of methyl (or ethyl) hydrazinocarboxylate and dithioester **7** (1.0 equivalent) in methylene chloride was heated at reflux for 2 hours and then concentrated *in vacuo*, followed by additional concentration under high vacuum. The crude **8**, after chromatography over a short column of silica gel or magnesium trisilicate with methylene chloride, was crystallized from the appropriate solvents, as described in Table I.

General Procedure for the Preparation of Alkanethioic Acid 2-(Aminocarbonyl)hydrazides **9** (N_3-Thioacylsemicarbazides).

Method A (Water Soluble).

A mixture of semicarbazide hydrochloride, sodium acetate trihydrate (1.05 equivalents), dithioester **7** (1.0 equivalent), water (*ca.* 5 ml/g semicarbazide hydrochloride), and ethanol (100 ml) was kept at 50° for 6 hours and concentrated *in vacuo*. The semisolid reaction mixture was then dried azeotropically *in vacuo* with several portions of ethanol (500 ml x 3) and then extracted in a Soxhlet extractor with absolute ethanol for 48 hours. The extract was filtered and concentrated *in vacuo* and the residue was crystallized from ethyl acetate-ethanol.

Method B (Organic Soluble).

The same procedure (*cf.* Method A) was used, but the concentrated reaction mixture was partitioned thrice with ethyl acetate and water. The combined ethyl acetate extract was then washed with saturated sodium chloride, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The residue was then crystallized from the appropriate solvents, as described in Table I.

Determination of pK_a Values for **8** and **9**.

A solution of *ca.* 75 mg of **8** (or **9**) in methanol (50 ml) was titrated with 0.0956 *N* sodium hydroxide (aqueous) in a Metrohm Titroprocessor 636. Since the titrant was in water, the solvent mixture was *ca.* 95-98% methanol at the midpoint of the titration. The pK_a' values were then corrected for solvent differences (methanol *vs.* water). The correction factor was determined by titration of benzoic acid in the above medium and comparing to the literature pK_a (water). The pK_a values of **8-9** approximate that of typical carboxylic acids [compound (pK_a)]: **8a** (4.70); **8c** (4.77); **8f** (4.39); **8k** (4.07); **8l** (4.38); **8n** (4.07); **8q** (4.63); **9c** (4.72).

General Procedure for the Preparation of **11** [Y = $COOCH_3$ (thiocarbazonate esters)], **12** [Y = $CONH_2$ (Thiosemicarbazonate Esters)], and **13** [Y = SO_2Aryl (Thiohydrazonate Esters)] from **8-10**.

Method A. Methyl [1-[(3-Methoxy-3-oxopropyl)thio]ethylidene]hydrazinocarboxylate (**11a**, R = H, R' = $(CH_2)_2COOCH_3$, Y = $COOCH_3$).

A mixture of methyl 2-(1-thioxoethyl)hydrazinocarboxylate (**8a**, 14.8 g, 100 mmoles), distilled methyl acrylate (17.2 g, 200 mmoles), dry triethylamine (2 ml), and anhydrous benzene (250 ml) was heated at reflux for 18 hours and concentrated *in vacuo*. The oily residue was chromatographed over silica gel [40 mm (w) x 300 mm (h)] with a gradient of 0-5% methanol in methylene chloride to afford a faint yellow oil. Crystallization from *t*-butyl methyl ether afforded the *Z*-isomer **11Za** as a white solid, 19.1 g (82%): mp 61.0-62.0°; ir (potassium bromide): 1730, 1700, 1450-1460 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.99 (s, 3H, $CH_3C=N$), 2.80 (t, 2H, J = 6.9 Hz, SCH_2CH_2), 3.23 (t, 2H, SCH_2), 3.70 (s, 3H, CH_3O), 3.78 (s, 3H, CH_3O), 7.99 (bs, 1H, NH). Concentration of the filtrate yielded the *E*-isomer **11Ea** as a faint yellow oil, 1.2 g (5%); ^{1}H nmr (90 MHz, deuteriochloroform): δ 2.31 (s, 3H, $CH_3C=N$), 2.71 (t, 2H, J = 7.2 Hz, SCH_2CH_2), 3.22 (t, 2H, SCH_2), 3.71 (s, 3H, CH_3O), 3.79 (s, 3H, CH_3O), 8.05 (bs, 1H, NH).

Anal. Calcd. for $C_8H_{14}N_2O_4S$: C, 41.02; H, 6.02; N, 11.96; S, 13.69. Found (**11Ea**): C, 40.97; H, 6.08; N, 11.97; S, 13.78. Found (**11Za**): C, 40.89; H, 6.11; N, 12.11; S, 13.85.

Method B.

A mixture of **8** (or **9**) (1 equivalent), the appropriate alkyl halide (1.1 equivalents), anhydrous potassium carbonate (2 equivalents), and acetone or acetonitrile (10 ml/g of **8** or **9**) was heated at reflux for 12-18 hours and concentrated *in vacuo*. The semisolid residue was extracted with boiling methylene chloride (or chloroform) and the extract chromatographed over silica gel (*cf.* Method A).

Methyl [1-[(3-Ethoxy-3-oxopropyl)thio]ethylidene]hydrazinocarboxylate (**11b**, R = H, R' = $(CH_2)_2COOC_2H_5$, Y = $COOCH_3$).

Z-Isomer (**11Zb**).

This compound was obtained as white crystals (diisopropyl ether), mp 36.0-38.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.27 (t, 3H *J* = 7.1 Hz, OCH_2CH_3), 1.99 (s, 3H, $CH_3C=N$), 2.71 (t, 2H, *J* = 7.3 Hz, SCH_2CH_2), 3.17 (t, 2H, SCH_2), 3.75 (s, 3H, CH_3O), 4.12 (q, 2H, OCH_2), 8.00 (bs, 1H, NH).

E-Isomer (**11Eb**).

This compound was obtained as a yellow oil; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.27 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3), 2.29 (s, 3H, $CH_3C=N$), 2.61 (t, 2H, *J* = 7.3 Hz, SCH_2CH_2), 3.17 (t, 2H, SCH_2), 3.78 (s, 3H, CH_3O), 4.13 (q, 2H, OCH_2), 8.05 (bs, 1H, NH).

Anal. Calcd. for $C_9H_{16}N_2O_4S$: C, 43.54; H, 6.50; N, 11.28; S, 12.91. Found (**11Eb**): C, 43.25; H, 6.45; N, 11.05; S, 12.75. Found (**11Zb**): C, 43.31; H, 6.55; N, 11.20; S, 12.97.

Methyl [1-[(3-Methoxy-3-oxopropyl)thio]-3,3-dimethylbutylidene]hydrazinocarboxylate (**11c**, R = *t*-butyl, R' = $(CH_2)_2COOCH_3$, Y = $COOCH_3$).

Z-Isomer (**11Zc**).

This was obtained as a yellow oil; ir (film): 1755-1720, 1568 cm^{-1}; ^{1}H nmr (300 MHz, deuteriochloroform): δ 1.02 (s, 9H, *t*-butyl), 2.46 (s, 2H, $CH_2C=N$), 2.58 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 3.11 (t, 2H, SCH_2), 3.71 (s, 3H, CH_3O), 3.82 (s, 3H, CH_3O), 8.52 (bs, 1H, NH).

E-Isomer (**11Ec**).

This was obtained as a yellow oil; ^{1}H nmr (300 MHz, deuteriochloroform): δ 1.04 (s, 9H, *t*-butyl), 2.24 (s, 2H, $CH_2C=N$), 2.81 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 3.23 (t, 2H, SCH_2), 3.70 (s, 3H, CH_3O), 3.80 (s, 3H, CH_3O), 7.80 (bs, 1H, NH).

Anal. Calcd. for $C_{12}H_{22}N_2O_4S$: C, 49.64; H, 7.64; N, 9.65; S, 11.04. Found (**11Ec-11Zc**): C, 49.48; H, 7.65; N, 9.74; S, 11.13.

Methyl [1-[(3-Ethoxy-3-oxopropyl)thio]-2-phenylethylidene]hydrazinocarboxylate (**11d**, R = C_6H_5, R' = $(CH_2)_2COOC_2H_5$, Y = $COOCH_3$).

This compound was obtained as an isomeric mixture. *Z*-Isomer (**11Zd**); ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.26 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3), 2.43 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 3.00 (t, 2H, SCH_2), 3.85 (s, 3H, CH_3O), 3.91 (s, 2H, $CH_2C=N$), 4.15 (q, 2H, OCH_2), 7.25 (m, 5H, C_6H_5), 8.38 (bs, 1H, NH); *E*-Isomer (**11Ed**); ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.28 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3), 2.82 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 3.31 (t, 2H, SCH_2), 3.59 (s, 2H, $CH_2C=N$), 3.73 (s, 3H, CH_3O), 4.16 (q, 2H, OCH_2), 7.25 (m, 5H, C_6H_5), 7.75 (bs, 1H, NH).

Anal. Calcd. for $C_{15}H_{20}N_2O_4S$: C, 55.54; H, 6.22; N, 8.63; S, 9.88. Found (**11Ed-11Zd**): C, 55.26; H, 6.15; N, 8.55; S, 10.01.

Methyl [1-[(3-Ethoxy-3-oxopropyl)thio]-2-(4-methylphenyl)ethylidene]hydrazinocarboxylate (**11e**, R = 4-$CH_3C_6H_4$, R' = $(CH_2)_2COOC_2H_5$, Y = $COOCH_3$).

This compound was obtained as an isomeric mixture; *Z*-Isomer (**11Ze**); ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.27 (t, 3H, *J* = 7.0 Hz, OCH_2CH_3), 2.36 (s, 3H, aryl-CH_3), 2.42 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 2.99 (t, 2H, SCH_2), 3.86 (s, 3H, CH_3O), 3.90 (s, 2H, $CH_2C=N$), 4.14 (q, 2H, OCH_2), 7.18 (m, 4H, C_6H_4), 8.41 (bs, 1H, NH); *E*-Isomer (**11Ee**). ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.27 (t, 3H, *J* = 7.0 Hz, OCH_2CH_3), 2.36 (s, 3H, aryl-CH_3), 2.81 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 3.30 (t, 2H, SCH_2), 3.60 (s, 2H, $CH_2C=N$), 3.74 (s, 3H, CH_3O), 4.15 (q, 2H, OCH_2), 7.18 (m, 4H, C_6H_4), 7.71 (bs, 1H, NH).

Anal. Calcd. for $C_{16}H_{22}N_2O_4S$: C, 56.79; H, 6.55; N, 8.27; S, 9.48. Found (**11Ee-11Ze**): C, 57.10; H, 6.66; N, 8.37; S, 9.75.

Methyl [1-[(3-Ethoxy-3-oxopropyl)thio]-2-(4-*t*-butylphenyl)ethylidene]hydrazinocarboxylate (**11f**, R = 4-*t*-butylC_6H_4, R' = $(CH_2)_2COOC_2H_5$, Y = $COOCH_3$).

Z-Isomer (**11Zf**).

This compound was obtained as a yellow oil; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.26 (t, 3H, *J* = 7.0 Hz, OCH_2CH_3), 1.33 (s, 9H, *t*-butyl), 2.38 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 2.99 (t, 2H, SCH_2), 3.84 (s, 3H, CH_3O), 3.89 (s, 2H, $CH_2C=N$), 4.14 (q, 2H, OCH_2), 7.22 (m, 4H, C_6H_4), 8.41 (bs, 1H, NH).

E-Isomer (**11Ef**).

This compound was obtained as white cubes (diisopropyl ether), mp 77.5-78.0°; ir (potassium bromide): 1715, 1670, 1595, 1500 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.26 (t, 3H, *J* = 7.0 Hz, OCH_2CH_3), 1.33 (s, 9H, *t*-butyl), 2.80 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 3.29 (t, 2H, SCH_2), 3.60 (s, 2H, $CH_2C=N$), 3.73 (s, 3H, CH_3O), 4.18 (q, 2H, OCH_2), 7.15-7.40 (m, 4H, C_6H_4), 7.71 (bs, 1H, NH).

Anal. Calcd. for $C_{19}H_{28}N_2O_4S$: C, 59.98; H, 7.42; N, 7.36; S, 8.43. Found (**11Ef**): C, 60.10; H, 7.35; N, 7.42; S, 8.32.

Methyl [1-[3-Ethoxy-3-oxopropyl)thio]-2-(3-methoxyphenyl)ethylidene]hydrazinocarboxylate (**11g**, R = 3-$CH_3OC_6H_4$, R' = $(CH_2)_2COOC_2H_5$, Y = $COOCH_3$).

This compound was obtained as an isomeric mixture; *Z*-Isomer (**11Zg**); ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.24 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3), 2.43 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 3.00 (t, 2H, SCH_2), 3.80 (s, 3H, CH_3O), 3.83 (s, 3H, CH_3O), 3.89 (s, 2H, $CH_2C=N$), 4.14 (q, 2H, OCH_2), 6.80-7.25 (m, 4H, C_6H_4), 8.45 (bs, 1H, NH); *E*-Isomer (**11Eg**); ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.23 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3), 2.79 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 3.28 (t, 2H, SCH_2), 3.64 (s, 2H, $CH_2C=N$), 3.75 (s, 3H, CH_3O), 3.80 (s, 3H, CH_3O), 4.15 (q, 2H, OCH_2), 6.80-7.25 (m, 4H, C_6H_4), 7.78 (bs, 1H, NH).

Anal. Calcd. for $C_{16}H_{22}N_2O_5S$: C, 54.23; H, 6.26; N, 7.90; S, 9.05. Found (**11Eg-11Zg**): C, 54.05; H, 6.15; N, 8.00; S, 9.18.

Methyl [1-[(3-Ethoxy-3-oxopropyl)thio]-2-(3,4,5-trimethoxyphenyl)ethylidene]hydrazinocarboxylate (**11h**, R = 3,4,5-$(CH_3O)_3C_6H_2$, R' = $(CH_2)_2COOC_2H_5$, Y = $COOCH_3$).

This compound was obtained as an isomeric mixture; *Z*-Isomer (**11Zh**); ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.27 (t, 3H, *J* = 7.0 Hz, OCH_2CH_3), 2.42 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 3.03 (t, 2H, SCH_2), 3.80-3.90 (bs, 12H, CH_3O x 4), 3.90 (s, 2H, $CH_2C=N$), 4.13 (q, 2H, OCH_2), 6.42 (s, 2H, C_6H_2), 8.47 (bs, 1H, NH); *E*-Isomer (**11Eh**); ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.27 (t, 3H, *J* = 7.0 Hz, OCH_2CH_3), 2.76 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 3.29 (t, 2H, SCH_2), 3.58 (s, 2H, $CH_2C=N$), 3.71 (s, 3H, $NHCOOCH_3$), 3.80-3.90 (bs, 9H, CH_3O x 3), 4.13 (q, 2H, OCH_2), 6.41 (s, 2H, C_6H_2), 7.72 (bs, 1H, NH).

Anal. Calcd. for $C_{18}H_{26}N_2O_7S$: C, 52.16; H, 6.32; N, 6.76; S, 7.74. Found (**11Eh-11Zh**): C, 51.98; H, 6.48; N, 6.80; S, 7.79.

Methyl [1-[(3-Ethoxy-3-oxopropyl)thio]-2-(4-chlorophenyl)ethylidene]hydrazinocarboxylate (**11i**, R = 4-ClC_6H_4, R' = $(CH_2)_2COOC_2H_5$, Y = $COOCH_3$).

This compound was obtained as an isomeric mixture; *Z*-Isomer (**11Zi**); ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.25 (t, 3H, *J* = 7.0 Hz, OCH_2CH_3), 2.47 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 3.00 (t, 2H, SCH_2), 3.87 (s, 3H, CH_3O), 3.90 (s, 2H, $CH_2C=N$), 4.15 (q, 2H, OCH_2), 7.30 (bs, 4H, C_6H_4), 8.48 (bs, 1H, NH); *E*-Isomer (**11Ei**); ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.25 (t, 3H, *J* = 7.0 Hz, OCH_2CH_3), 2.80 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 3.30 (t, 2H, SCH_2), 3.64 (s, 2H, $CH_2C=N$), 3.76 (s, 3H, CH_3O), 4.15 (q, 2H, OCH_2), 7.30 (bs, 4H, C_6H_4), 7.75 (bs, 1H, NH).

Anal. Calcd. for $C_{15}H_{20}ClN_2O_4S$: C, 50.07; H, 5.60; Cl, 9.85; N, 7.78; S, 8.91. Found (**11Ei-11Zi**): C, 50.25; H, 5.48; Cl, 9.57; N, 7.71; S, 8.64.

Methyl [1-[(3-Ethoxy-3-oxopropyl)thio]-2-(4-fluorophenyl)ethylidene]hydrazinocarboxylate (**11j**, R = 4-FC_6H_4, R' = $(CH_2)_2COOC_2H_5$, Y = $COOCH_3$).

Z-Isomer (**11Zj**).

This compound was obtained as a yellow oil; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.27 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3), 2.43 (t, 2H, *J* = 7.2

Hz, SCH_2CH_2), 2.98 (t, 2H, SCH_2), 3.87 (s, 3H, CH_3O), 3.91 (s, 2H, $CH_2C=N$), 4.15 (q, 2H, OCH_2), [7.00 (dd, 2H, $J = {}^3J_{H,F} = 9.0$ Hz) and 7.23 (dd, 2H, ${}^4J_{H,F} = 5.8$ Hz, $J = 9.0$ Hz) (C_6H_4)], 8.45 (bs, 1H, NH).

E-Isomer (**11Ej**).

This compound was obtained as a yellow oil; ¹H nmr (90 MHz, deuteriochloroform): δ 1.27 (t, 2H, $J = 7.1$ Hz, OCH_2CH_3), 2.81 (t, 2H, $J = 7.2$ Hz, SCH_2CH_2), 3.28 (t, 2H, SCH_2), 3.69 (s, 2H, $CH_2C=N$), 3.76 (s, 3H, CH_3O), 4.16 (q, 2H, OCH_2), [7.01 (dd, 2H, $J = {}^3J_{H,F} = 9.0$ Hz) and 7.21 (dd, 2H, ${}^4J_{H,F} = 5.8$ Hz, $J = 9.0$ Hz) (C_6H_4)], 8.15 (bs, 1H, NH).

Anal. Calcd. for $C_{15}H_{20}FN_2O_4S$: C, 52.47; H, 5.88; F, 5.53; N, 8.15; S, 9.34. Found (**11Ej**): C, 52.15; H, 6.01; F, 5.61; N, 7.99; S, 9.51

Methyl [1-[(3-Ethoxy-3-oxopropyl)thio]-2-[(2-naphthyl)ethylidene]hydrazinocarboxylate (**11k**, R = 2-naphthyl, R' = $(CH_2)_2COOC_2H_5$, Y = $COOCH_3$).

Z-Isomer (**11Zk**).

This was obtained as a yellow oil; ¹H nmr (90 MHz, deuteriochloroform): δ 1.23 (t, 3H, $J = 7.1$ Hz, OCH_2CH_3), 2.42 (t, 2H, $J = 7.2$ Hz, SCH_2CH_2), 3.03 (t, 2H, SCH_2), 3.93 (s, 3H, CH_3O), 4.13 (q, 2H, OCH_2), 4.15 (s, 2H, $CH_2C=N$), 7.25-7.95 (m, 7H, $C_{10}H_7$), 8.50 (bs, 1H, NH).

E-Isomer (**11Ek**).

This was obtained as a yellow oil; ¹H nmr (90 MHz, deuteriochloroform): δ 1.23 (t, 3H, $J = 7.1$ Hz, OCH_2CH_3), 2.84 (t, 2H, $J = 7.2$ Hz, SCH_2CH_2), 3.35 (t, 2H, SCH_2), 3.74 (s, 3H, CH_3O), 3.84 (s, 2H, $CH_2C=N$), 4.14 (q, 2H, OCH_2), 7.25-7.95 (m, 7H, $C_{10}H_7$), 7.90 (bs, 1H, NH).

Anal. Calcd. for $C_{19}H_{22}N_2O_4S$: C, 60.95; H, 5.92; N, 7.48; S, 8.56. Found (**11Ek**): C, 60.76; H, 5.89; N, 7.64; S, 8.81. Found (**11Zk**): C, 60.87; H, 6.05; N, 7.35; S, 8.76.

(±) Methyl [1-[(3-Methoxy-3-oxopropyl)thio]-2-[(tetrahydro-2*H*-pyran-2-yl)ethylidene]hydrazinocarboxylate (**11l**, R = 2-C_5H_9O, R' = $(CH_2)_2COOCH_3$, Y = $COOCH_3$).

Z-Isomer (**11Zl**).

This compound was obtained as a yellow oil; ir (film): 1745, 1720, 1600 cm⁻¹; ¹H nmr (300 MHz, deuteriochloroform): δ 1.25-1.90 [m, 6H, $OCH_2(CH_2)_3$], [2.30 (dd, 1H, $J_{gem} = 14.7$ Hz, $J = 2.0$ Hz) and 2.63 (dd, 1H, $J_{gem} = 14.7$ Hz, $J = 8.4$ Hz) ($CH_2C=N$)], 2.81 (t, 2H, $J = 6.6$ Hz, SCH_2CH_2), 3.25 (t, 2H, SCH_2), 3.42-3.57 (m, 2H, OCH_2), 3.70 (s, 3H, CH_3O), 3.76 (s, 3H, CH_3O), 4.03 (d, 1H, $OCHCH_2$), 9.65 (bs, 1H, NH).

E-Isomer (**11El**).

This compound was obtained as a yellow oil; ir (film): 1740-1720, 1585 cm⁻¹; ¹H nmr (300 MHz, deuteriochloroform): δ 1.25-1.90 [m, 6H, $OCH_2(CH_2)_3$], 2.62 (t, 2H, $J = 7.2$ Hz, SCH_2CH_2), 2.65-2.80 (m, 2H, $CH_2C=N$), 3.18 (t, 2H, SCH_2), 3.42 (dt, 2H, OCH_2), 3.73 (s, 3H, CH_3O), 3.83 (s, 3H, CH_3O), 3.94 (bd, 1H, $OCHCH_2$), 8.42 (bs, 1H, NH).

Anal. Calcd. for $C_{13}H_{22}N_2O_5S$: C, 49.04; H, 6.97; N, 8.80; S, 10.07. Found (**11El**): C, 48.89; H, 6.85; N, 8.78; S, 10.40. Found (**11Zl**): C, 48.89; H, 6.88; N, 8.94; S, 10.42.

Methyl [1-[(2-Cyanoethyl)thio]-2-phenylethylidene]hydrazinocarboxylate (**11m**, R = C_6H_5, R' = CH_2CH_2CN, Y = $COOCH_3$).

This compound was obtained as an isomeric mixture; *Z*-Isomer (**11Zm**); ¹H nmr (90 MHz, deuteriochloroform): δ 2.35 (t, 2H, $J = 7.2$ Hz, CH_2CN), 2.98 (t, 2H, SCH_2), 3.88 (s, 3H, CH_3O), 3.93 (s, 2H, $CH_2C=N$), 7.28 (bs, 5H, C_6H_5), 8.34 (bs, 1H, NH); *E*-Isomer (**11Em**); ¹H nmr (90 MHz, deuteriochloroform): δ 2.95 (t, 2H, $J = 7.2$ Hz, CH_2CN), 3.28 (t, 2H, SCH_2), 3.65 (s, 2H, $CH_2C=N$), 3.75 (s, 3H, CH_3O), 7.28 (bs, 5H, C_6H_5), 7.79 (bs, 1H, NH).

Anal. Calcd. for $C_{13}H_{15}N_3O_2S$: C, 56.30; H, 5.45; N, 15.15; S, 11.56. Found (**11Em-11Zm**): C, 56.25; H, 5.49; N, 14.99; S, 11.67.

Ethyl 3-[[1-(Aminocarbonyl)hydrazono]propyl]thio]propanoate (**12a**, R = CH_3, R' = $(CH_2)_2COOC_2H_5$, Y = $CONH_2$).

Z-Isomer (**12Za**).

This compound was obtained as white crystals (diisopropyl ether), mp 63.5-64.5°; ir (potassium bromide): 3465, 1735, 1695, 1575, 1180 cm⁻¹; ¹H nmr (90 MHz, deuteriochloroform): δ 1.16 (t, 3H, $J = 7.1$ Hz, $CH_3CH_2C=N$), 1.25 (t, 3H, $J = 7.2$ Hz, OCH_2CH_3), 2.51 (q, 2H, $CH_2C=N$), 2.59 (t, 2H, $J = 6.5$ Hz, SCH_2CH_2), 3.14 (t, 2H, SCH_2), 4.15 (q, 2H, OCH_2), 5.71 (bs, 2H, NH_2), 8.12 (bs, 1H, NH).

Anal. Calcd. for $C_9H_{17}N_3O_3S$: C, 43.71; H, 6.93; N, 16.99; S, 12.97. Found (**12Za**): C, 43.66; H, 6.91; N, 17.29; S, 13.06.

Ethyl 3-[[1-[(Aminocarbonyl)hydrazono]butyl]thio]propanoate (**12b**, R = CH_3CH_2, R' = $(CH_2)_2COOC_2H_5$, Y = $CONH_2$).

Z-Isomer (**12Zb**).

This compound was obtained as white crystals (diisopropyl ether), mp 38.5-39.5°; ir (potassium bromide): 3450, 1735, 1685, 1575, 1245, 1180 cm⁻¹; ¹H nmr (90 MHz, deuteriochloroform): δ 0.99 [t, 3H, $J = 7.6$ Hz, $CH_3(CH_2)_2$], 1.29 (t, 3H, $J = 7.5$ Hz, OCH_2CH_3), 1.70 (m, 2H, $CH_3CH_2CH_2$), 2.51 (t, 2H, $CH_2C=N$), 2.62 (t, 2H, $J = 7.2$ Hz, SCH_2CH_2), 3.13 (t, 2H, SCH_2), 4.16 (q, 2H, OCH_2), 5.50 (bs, 2H, NH_2), 8.05 (bs, 1H, NH).

Anal. Calcd. for $C_{10}H_{19}N_3O_3S$: C, 45.96; H, 7.33; N, 16.08; S, 12.27. Found (**12Zb**): C, 46.31; H, 7.26; N, 16.46; S, 12.57.

Methyl 3-[[1-[(Aminocarbonyl)hydrazono]-3-phenylpropyl]thio]propanoate (**12c**, R = $C_6H_5CH_2$, R' = $(CH_2)_2COOCH_3$, Y = $CONH_2$).

Z-Isomer (**12Zc**).

This compound was obtained as a yellow oil; ir (film): 3460, 1735, 1690, 1570, 1440 cm⁻¹; ¹H nmr (300 MHz, deuteriochloroform): δ 2.59 (t, 2H, $J = 7.2$ Hz, SCH_2CH_2), 2.80 (t, 2H, $J = 8.1$ Hz, $CH_2C=N$), 2.97 (t, 2H, $C_6H_5CH_2$), 3.13 (t, 2H, SCH_2), 3.71 (s, 3H, CH_3O), 4.80 (bs, 2H, NH_2), 8.03 (bs, 1H, NH).

E-Isomer (**12Ec**).

This compound was obtained as a yellow oil; ¹H nmr (300 MHz, deuteriochloroform): δ 2.60 (t, 2H, $J = 8.1$ Hz, $CH_2C=N$), 2.69 (t, 2H, $J = 7.2$ Hz, SCH_2CH_2), 2.88 (t, 2H, $C_6H_5CH_2$), 3.16 (t, 2H, SCH_2), 3.70 (s, 3H, CH_3O), 4.80 (bs, 2H, NH_2), 7.64 (bs, 1H, NH).

Anal. Calcd. for $C_{14}H_{14}N_3O_3S$: C, 55.25; H, 4.64; N, 13.80; S, 10.54. Found (**12Ec**): C, 55.45; H, 4.61; N, 13.85; S, 10.51. Found (**12Zc**): C, 55.35; H, 4.65; N, 13.91; S, 10.42.

Ethyl 3-[[1-[[(4-Methylphenyl)sulfonyl]hydrazono]propyl]thio]propanoate (**13a**, R = CH_3, R' = $(CH_2)_2COOC_2H_5$, Y = 4-$CH_3C_6H_4SO_2$).

Z-Isomer (**13Za**).

This compound was obtained as a yellow oil; ir (film): 3179, 1735, 1345, 1172, 734, 670, 580 cm⁻¹; ¹H nmr (300 MHz, deuteriochloroform): δ 1.12 (t, 2H, $J = 7.4$ Hz, $CH_3CH_2C=N$), 1.27 (t, 3H, $J = 7.2$ Hz, OCH_2CH_3), 2.43 (s, 3H, aryl-CH_3), 2.47 (q, 2H, $CH_2C=N$), 2.51 (t, 2H, CH_2CO_2), 3.08 (t, 2H, SCH_2), 4.15 (q, 2H, OCH_2), [7.31 (d, 2H, $J = 8.4$ Hz) and 7.82 (d, 2H) (C_6H_4)], 7.84 (bs, 1H, NH).

E-Isomer (**13Ea**).

This compound was obtained as white crystals (*t*-butyl methyl ether), mp 80.0-81.0°; ¹H nmr (300 MHz, deuteriochloroform): δ 1.09 (t, 2H, $J = 7.6$ Hz, $CH_3CH_2C=N$), 1.28 (t, 3H, $J = 7.1$ Hz, OCH_2CH_3), 2.32 (q, 2H, $CH_2C=N$), 2.44 (s, 3H, aryl-CH_3), 2.54 (t, 2H, CH_2CO_2), 3.00 (t, 2H, SCH_2), 4.17 (q, 2H, OCH_2) [7.33 (d, 2H, $J = 7.1$ Hz) and 7.84 (d, 2H) (C_6H_4)], 7.76 (s, 1H, NH).

Anal. Calcd. for $C_{15}H_{22}N_2O_4S_2$: C, 50.26; H, 6.19; N, 7.81; S, 17.89. Found (**13Za**): C, 50.21; H, 6.35; N, 7.61; S, 17.75. Found (**13Ea**): C, 50.25; H, 6.23; N, 7.65; S, 17.84.

General Procedure for Preparation of Methyl (or Ethyl) Dithioalkanoates **14** from 1-[1-(Alkylthio)alkylidene]piperidinium Iodides.

A mixture of *N*-thioacylpiperidide **4** and methyl (or ethyl) iodide (1.10 equivalents) in anhydrous ether (5 ml/g *N*-thioacylpiperidide) was stirred at ambient temperature for 12 hours. The solvent was decanted from the hygroscopic salt and substituted with a similar quantity of absolute ethanol. The faint yellow solution was treated with hydrogen sulfide (1.5 equivalents) at ambient temperature. After 12 hours at ambient temperature, the solvent was evaporated *in vacuo* and the semicrystalline residue was taken up into anhydrous ether, filtered, and concentrated *in vacuo*. The crude dithioesters **14** were then distilled (all yields were >70%).

Methyl Benzeneethane(dithioate) (**14a**).

This compound was obtained as a yellowish-orange liquid, bp 98.0-100.0°/0.4 mm Hg; ^{1}H nmr (90 MHz, deuteriochloroform): δ 2.61 (s, 3H, CH_3S), 4.36 (s, $2H_2CS$), 7.34 (bs, 5H, C_6H_5).

Anal. Calcd. for $C_9H_{10}S_2$: C, 59.30; H, 5.53; S, 35.17. Found: C, 59.05; H, 5.61; S, 35.38.

Methyl 4-Fluorobenzeneethane(dithioate) (**14b**).

This compound was obtained as an orange liquid, bp 95.0-96.0°/0.4 mm Hg; ir (film): 1505, 1215 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 2.62 (s, 3H, CH_3S), 4.32 (s, 2H, CH_2CS), [7.01 (dd, 2H, J = $^3J_{H,F}$ = 9.0 Hz) and 7.38 (dd, 2H, $^4J_{H,F}$ = 5.5 Hz, J = 9.0 Hz) (C_6H_4)].

Anal. Calcd. for C_9H_9FS: C, 53.97; H, 4.53; F, 9.49; S, 32.02. Found: C, 54.24; H, 4.64; F, 9.36; S, 31.90.

Methyl 4-Methoxybenzeneethane(dithioate) (**14c**).

This compound was obtained as an orange liquid, bp 115.0-116.0°/0.2 mm Hg; ir (film): 1605, 1510, 1250 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 2.58 (s, 3H, CH_3S), 3.77 (s, 3H, CH_3O), 4.28 (s, 2H, CH_2CS), [6.85 (d, 2H, J = 8.0 Hz) and 7.26 (d, 2H) (C_6H_4)].

Anal. Calcd. for $C_{10}H_{12}OS_2$: C, 56.57; H, 5.70; S, 30.20. Found: C, 56.42; H, 5.69; S, 29.83.

Methyl 2-Thiopheneethane(dithioate) (**14d**).

This compound was obtained as a yellowish-orange liquid, bp 98.5-99.5°/0.4 mm Hg; ir (film): 1737, 1415, 1215, 1150, 700 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 2.62 (s, 3H, CH_3S), 4.52 (s, 2H, CH_2CS), [7.01 (m, 2H) and 7.22 (m, 1H) (C_4H_3S)].

Anal. Calcd. for $C_7H_8S_3$: C, 44.64; H, 4.28; S, 51.08. Found: C, 45.01; H, 4.25; S, 50.99.

Methyl 3-Ethoxy-3-oxopropane(dithioate) (**14e**).

This compound was obtained as a yellowish-orange liquid, bp 91.0-92.0°/1.0 mm Hg; ir (film): 1738, 1300, 1255, 1190 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.27 (t, 3H, J = 7.0 Hz, CH_3CH_2O), 2.65 (s, 3H, CH_3S), 4.00 (s, 2H, CH_2CS_2), 4.19 (q, 2H, OCH_2).

Anal. Calcd. for $C_6H_{10}O_2S_2$: C, 40.43; H, 5.65; S, 35.97. Found: C, 40.67; H, 5.62; S, 35.85.

Ethyl Ethane(dithioate) (**14f**) and Ethyl Propane(dithioate) (**14g**).

These esters were prepared by the procedure of Meijer, Vermeer, and Brandsma [27].

General Procedure for Preparation of **8** and **11** from Methyl (or Ethyl) Dithioalkanoates (**14**).

A mixture of methyl (or ethyl) hydrazinocarboxylate and dithioalkanoate **14** (1.0 equivalent) in methylene chloride was heated at reflux for 4 hours and then concentrated *in vacuo*. The reaction mixture was then partitioned thrice between methylene chloride and 0.5 *M* sodium carbonate. The aqueous alkaline extract was acidified to *p*H 3 and **8** was recovered by methylene chloride extraction and subsequent crystallization (see Table I). The neutral organic fraction was dried over anhydrous sodium sulfate, concentrated, and chromatographed over silica gel 60 (0 to 5% methanol-methylene chloride) to afford **11**. Separation of the isomeric thiocarbazonate esters could be accomplished by either fractional crystallization or silica gel chromatography.

Methyl [1-(Ethylthio)ethylidene]hydrazinocarboxylate (**11n**, R = H, R' = CH_2CH_3, Y = $COOCH_3$).

Z-Isomer (**11Zn**).

This compound was obtained as white needles (methylcyclohexane), mp 90.0-90.5°; ir (potassium bromide): 1725, 1700, 1550 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.26 (t, 3H, J = 6.9 Hz, CH_3CH_2S), 1.93 (s, 3H, $CH_3C=N$), 2.91 (q, 2H, SCH_2), 3.67 (s, 3H, CH_3O), 7.62 (bs, 1H, NH).

Anal. Calcd. for $C_6H_{12}N_2O_2S$: C, 40.89; H, 6.86; N, 15.89; S, 18.19. Found (**11Zn**): C, 40.62; H, 6.60; N, 15.92; S, 18.40.

Methyl [1-(Ethylthio)propylidene]hydrazinocarboxylate (**11o**, R = CH_3, R' = CH_2CH_3, Y = $COOCH_3$).

Z-Isomer (**11Zo**).

This compound was obtained as white needles (hexane), mp 60.0-60.5°; ir (potassium bromide): 1735, 1710, 1600, 1550 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.14 (t, 3H, J = 7.0 Hz, $CH_3CH_2C=N$), 1.30 (t, 3H, J = 7.2 Hz, CH_3CH_2S), 2.28 (q, 2H, $CH_2C=N$), 2.88 (q, 2H, SCH_2), 3.73 (s, 3H, CH_3O), 7.84 (bs, 1H, NH).

E-Isomer (**11Eo**).

This compound was obtained as a light yellow oil; ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.21 (t, 3H, J = 7.0 Hz, $CH_3CH_2C=N$), 1.28 (t, 3H, J = 7.2 Hz, CH_3CH_2S), 2.50 (q, 2H, $CH_2C=N$), 2.82 (q, 2H, SCH_2), 3.73 (s, 3H, CH_3O), 8.14 (s, 1H, NH).

Anal. Calcd. for $C_7H_{14}N_2O_2S$: C, 44.19; H, 7.42; N, 14.72; S, 16.85. Found (**11Eo**): C, 44.00; H, 7.25; N, 14.65; S, 16.92. Found (**11Zo**): C, 44.25; H, 7.45; N, 14.69; S, 16.75.

Methyl [2-[(4-Fluorophenyl)-1-(methylthio)ethylidene]hydrazinocarboxylate (**11p**, R = 4-FC_6H_4, R' = CH_3, Y = $COOCH_3$).

Z-Isomer (**11Zp**).

This compound was obtained as ivory needles (diisopropyl ether), mp 127.5-128.0°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 2.38 (s, 3H, CH_3S), 3.68 (s, 2H, $CH_2C=N$), 3.71 (s, 3H, CH_3O), [7.04 (d, 2H, J = $^3J_{H,F}$ = 9.0 Hz) and 7.22 (d, 2H, $^4J_{H,F}$ = 5.5 Hz, J = 9.0 Hz) (C_6H_4)], 7.25 (bs, 1H, NH).

E-Isomer (**11Ep**).

This was obtained as a yellow oil; ^{1}H nmr (90 MHz, deuteriochloroform): δ 2.25 (s, 3H, CH_3S), 3.81 (s, 3H, CH_3O), 3.90 (s, 2H, $CH_2C=N$), [7.04 (d, 2H, J = $^3J_{H,F}$ = 9.0 Hz) and 7.21 (d, 2H, $^4J_{H,F}$ = 5.5 Hz, J = 9.0 Hz) (C_6H_4)], 8.15 (bs, 1H, NH).

Anal. Calcd. for $C_{11}H_{13}FN_2O_2S$: C, 51.55; H, 5.11; F, 7.41; N, 10.93; S, 12.52. Found (**11Ep**): C, 51.35; H, 5.20; F, 7.75; N, 11.01; S, 12.65. Found (**11Zp**): C, 51.72; H, 5.00; F, 7.55; N, 11.06; S, 12.45.

Methyl [2-[(4-Methoxyphenyl)-1-(methylthio)ethylidene]hydrazinocarboxylate (**11q**, R = 4-$CH_3OC_6H_4$, R' = CH_3, Y = COOCH}).

This compound was obtained as an isomeric mixture; *Z*-Isomer (**11Zq**); ^{1}H nmr (90 MHz, deuteriochloroform): δ 2.40 (s, 3H, CH_3S), 3.61 (s, 2H, $CH_2C=N$), 3.71 (s, 3H, $NHCOOCH_3$), 3.78 (s, 3H, aryl-OCH_3), [6.85 (d, 2H) and 7.20 (d, 2H) (C_6H_4)], 7.80 (bs, 1H, NH); *E*-Isomer (**11Eq**); ^{1}H nmr (90 MHz, deuteriochloroform): δ 2.25 (s, 3H, CH_3S), 3.78 (s, 3H, aryl-OCH_3), 3.83 (s, 3H, $NHCOOCH_3$), 3.85 (s, 2H, $CH_2C=N$), [6.85 (d, 2H) and 7.21 (d, 2H) (C_6H_4)], 8.10 (bs, 1H, NH).

Anal. Calcd. for $C_{12}H_{16}N_2O_3S$: C, 53.71; H, 6.01; N, 10.44; S, 11.95. Found (**11Eq-11Zq**): C, 53.62; H, 5.99; N, 10.62; S, 12.02.

Methyl [(1-Methylthio)-2-(2-thienyl)ethylidene]hydrazinocarboxylate (**11r** R = 2-thienyl, R' = CH_3, Y = $COOCH_3$).

Z-Isomer (**11Zr**).

This compound was obtained as white crystals (diisopropyl ether), mp 119.5-121.0°; ir (potassium bromide): 1715, 1695, 1540 cm^{-1}; ^{1}H nmr (90 MHz, deuteriochloroform): δ 2.45 (s, 3H, CH_3S), 3.75 (s, 3H, CH_3O), 3.85 (s, 2H, $CH_2C=N$), [6.98 (m, 2H) and 7.25 (m, 1H) (C_4H_3S)], 7.25 (bs, 1H, NH).

Anal. Calcd. for $C_9H_{12}N_2O_2S$: C, 44.24; H, 4.95; N, 11.47; S, 26.25. Found (**11Zr**): C, 44.44; H, 4.93; N, 11.73; S, 26.15.

General Procedure for the Preparation of Methyl (or Ethyl) [1-(Alkylthio)-alkylidene]hydrazinocarboxylates **11** from Carbohydrazonoyl Halides **20**.

Ethyl [1-[(3-Ethoxy-3-oxopropyl)thio]ethylidenehydrazinocarboxylate (**11s**, R = H, R' = $C_2H_4COOC_2H_5$, Y = $COOC_2H_5$).

A mixture of ethyl 2-(acetyl)hydrazinocarboxylate (**16a**, 6.42 g, 44 mmoles) and phosphorus pentachloride (9.15 g, 44 mmoles) was maintained at 75-85° for 2.5 hours and then concentrated *in vacuo*. The crude ethyl 2-(1-chloroethylidene)hydrazinocarboxylate (**20a**) was dissolved in 150 ml of cold (5°) anhydrous tetrahydrofuran and treated with a cold solution (5°) of methanolic sodium methyl propionate-3-thiolate [sodium methoxide (2.4 g, 44 mmoles), methyl 3-mercaptopropionate (5.28 g, 44 mmoles), and absolute methanol (50 ml)]. After 2 hours, the solvent was removed *in vacuo* and the residue partitioned between water and methylene chloride twice. The organic extract was worked-up and chromatographed on silica gel 60 [35 mm (w) x 300 mm (h)] with a gradient of 0-2% methanol in methylene chloride. The resultant oily ester **11s** (6.60 g, 60%) consisted of a 4:1 ratio of **11Zs/11Es**-isomers. *Z*-Isomer (**11Zs**). ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.25 (t, 3H, *J* = 7.4 Hz, OCH_2CH_3), 2.00 (s, 3H, $CH_3C=N$), 2.80 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 3.24 (t, 2H, SCH_2), 3.69 (s, 3H, CH_3O), 4.10 (q, 2H, OCH_2), 7.97 (bs, 1H, NH); *E*-Isomer (**11Es**). ^{1}H nmr (90 MHz, deuteriochloroform): δ 1.28 (t, 3H, *J* = 7.4 Hz. OCH_2CH_3), 2.30 (s, 3H, $CH_3C=N$), 2.75 (t, 2H, *J* = 7.2 Hz, SCH_2CH_2), 3.23 (t, 2H, SCH_2), 3.72 (s, 3H, CH_3O), 4.12 (q, 2H, OCH_2), 8.03 (bs, 1H, NH).

Methyl [1-(Phenylthio)-3,3-dimethylbutylidene]hydrazinocarboxylate (**11t**, R = *t*-butyl, R' = C_6H_5, Y = $COOCH_3$).

This compound was prepared from methyl 2-(3,3-dimethylbutyryl)-hydrazinocarboxylate (**16b**) *via* the corresponding hydrazonoyl chloride **20b** to give *Z*-isomer (**11Zt**) in 66% yield as light yellow oil; ir (film): 1755, 1724, 1578 cm^{-1}; ^{1}H nmr (300 MHz, deuteriochloroform): δ 0.96 (s, 9H, *t*-butyl), 2.33 (s, 2H, $CH_2C=N$), 3.83 (s, 3H, CH_3O), 7.32 (bs, 5H, C_6H_5), 8.65 (bs, 1H, NH).

Anal. Calcd. for $C_{14}H_{20}N_2O_2S$: C, 59.97; H, 7.19; N, 9.99; S, 11.44. Found (**11Zt**): C, 59.74; H, 6.90; N, 9.96; S, 11.43.

Methyl [1-(Phenylthio)-2-phenylethylidene]hydrazinocarboxylate (**11u**, R = R' = C_6H_5, Y = $COOCH_3$).

This compound was prepared from methyl 2-(phenylacetyl)hydrazinocarboxylate (**16c**) *via* the corresponding hydrazonoyl chloride **20c** to give *Z*-isomer (**11Zu**) in 60% yield as lemon yellow crystals (diisopropyl ether), mp 67.5-70.0°; ir (potassium bromide): 1720, 1598 cm^{-1}; ^{1}H nmr (300 MHz, deuteriochloroform): δ 3.72 (s, 2H, $CH_2C=N$), 3.87 (s, 3H, CH_3O), [6.98 (m, 5H) and 7.20 (m, 5H) (H arom)], 8.45 (bs, 1H, NH).

Anal. Calcd. for $C_{16}H_{16}N_2O_2S$: C, 63.98; H, 5.37; N, 9.33; S, 10.67. Found (**11Zu**): C, 64.29; H, 5.46; N, 9.29; S, 10.50.

Single-Crystal X-ray Structure Determination of **11Ef** [28].

Crystals suitable for X-ray diffraction analysis were obtained by recrystallization of thiocarbazonate ester **11Ef** from diisopropyl ether. The crystal used for data collection was a colorless prism having dimensions of 0.15 x 0.20 x 0.25 mm. Lattice constants and intensity data were measured at 23° and λ = 1.54184 Å (Cu K_α) on an Enraf-Nonius CAD4 computer controlled kappa axis diffractometer equipped with a graphite crystal, incident beam monochromator. Data were collected to a maximum 2θ of 150°. A total of 4426 reflections were collected, of which 4275 were unique. Data reduction included corrections for Lorentz and polarization effects. No absorption or extinction corrections were applied. The space group was determined to be P1. Cell data: triclinic; a = 10.650 (s) Å, b = 10.915 (2) Å, c = 9.933 (1) Å, a = 99.53 (2)°, b = 105.31 (2)°, g = 105.44 (2)°, V = 1038.4 Å^3, ρ_C = 1.22 g cm^{-1}; Z = 2.

The structure was solved by direct methods, and calculations were performed on a PDP-11/60 based TEXRAY system. A total of 22 atoms were located from an E-map prepared from the phase set with probability statistics. The remaining atoms were located in succeeding difference Fourier syntheses. Hydrogen atoms were included in calculated positions (assuming idealized geometries with C-H = 0.95Å) and were not refined. The structure was refined in full-matrix least-squares where the function minimized was $\Sigma w(|Fo| - |Fc|)^2$ and the w is defined as $4Fo^2/\sigma^2(Fo^2)$. The standard deviation on intensities, $\sigma(Fo^2)$, is defined as follows: $\sigma^2(Fo^2)=[S^2(C + R^2B) + (pFo^2)^2]/Lp^2$ where S is the scan rate, C is the total integrated peak count, R is the ratio of scan time to background counting time, B is the total background count. Lp is the Lorentz-polarization factor, and the parameter p is a factor introduced to downweight intense reflections. Here p was set to 0.060.

Single-Crystal X-ray Structure Determination of **11Zu** [28].

Crystals suitable for X-ray diffraction analysis were obtained by recrystallization of thiocarbazonate ester **11Zu** from diisopropyl ether. The crystal used for data collection was a colorless needlelike crystal having dimensions of 0.10 x 0.15 x 0.30 mm. Lattice constants and intensity data were measured at 23° and λ = 1.54184 Å (Cu K_α) on an Enraf-Nonius CAD4 computer controlled kappa axis diffractometer equipped with a graphite crystal, incident beam monochromator. Data were collected to a maximum 2θ of 150°. A total of 3725 reflections were collected, of which 3145 were unique. Data reduction included corrections for Lorentz and polarization effects. No absorption or extinction corrections were applied. Systematic absences for Okl (k = 2n + 1), hOl (l = 2n + 1), and hkO (h = 2n + 1) unambiguously indicated the space group to be Pbca. Cell data: orthorhombic; a = 10.970 (3) Å, b = 8.293 (1) Å, c = 33.588 (7) Å, V = 3055.6 Å^3, ρ_C = 1.31 g cm^{-1}; Z = 8.

The structure was solved by direct methods, and calculations were performed on a PDP-11/60 based TEXRAY system. A total of 16 atoms were located from an E-map prepared from the phase set with probability statistics. The remaining atoms were located in succeeding difference Fourier syntheses. Hydrogen atoms were located and their positions and isotropic thermal parameters were refined. The structure was refined in full-matrix least-squares where the function minimized was $\Sigma w(|Fo| - |Fc|)^2$ and the w is defined as $4Fo^2/\sigma^2(Fo^2)$. The standard deviation on intensities, $\sigma(Fo^2)$, is defined as follows: $\sigma^2(Fo^2)=[S^2(C + R^2B) + (pFo^2)^2]/Lp^2$ where S is the scan rate, C is the total integrated peak count, R is the ratio of scan time to background counting time, B is the total background count. Lp is the Lorentz-polarization factor, and the parameter p is a factor introduced to downweight intense reflections. Here p was set to 0.050.

General Procedure for the Preparation of 1,2,3-Thiadiazoles **2-3**.

A mixture of **11-13** in methylene chloride (*ca.* 5 ml/g of ester) was treated, at 0° with thionyl chloride (2 equivalents). When the vigorous reaction subsided, the homogeneous mixture was heated at reflux for 2 hours and concentrated *in vacuo*. The smelly residue was partitioned thrice between methylene chloride and water; workup of the combined organic extract and chromatography over silica gel (ethyl acetate-petroleum ether or methylene chloride-petroleum ether) afforded thiadiazoles **2-3** of >95% purity. Crystallization, when possible, was accomplished with appropriate solvents, as described in Tables III and IV.

General Procedure for the Preparation of 1,2,3-Thiadiazole-4-thiolates **1**.

A cold ethanolic solution of thiadiazoles **2** was treated with freshly prepared ethanolic sodium (or potassium) ethoxide (0.95 equivalent). After 30 minutes, the solvent volume was reduced *in vacuo* (T <30°) to one-fourth of the original volume. This was then diluted with ten volumes of anhydrous ether and the precipitated thiolates **15** collected. Additional purification was accomplished by dissolving crude **1** in ethanol, decolorizing, concentrating to one-fourth volume, and reprecipitating with anhydrous ether (*cf.* Table VI).

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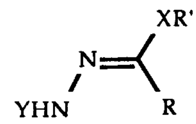
[17] The term "thiocarbazonate ester, *i*" derives from its relationship to the "carbazonate esters, **ii**". This is analogous to that of "thiohydrazonate ester, *iii*" *vs.* "hydrazonate ester, *iv*".



i R = alkyl, aryl, or hydrogen; R′ = alkyl or aryl; X = *sulfur*; Y = carboalkoxy

ii R = alkyl, aryl, or hydrogen; R′ = alkyl or aryl; X = *oxygen*; Y = carboalkoxy

iii R and Y = alkyl, aryl, or hydrogen; R′ = alkyl or aryl; X = *sulfur*

iv R and Y = alkyl, aryl, or hydrogen; R′ = alkyl or aryl; X = *oxygen*

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[28] Single-crystal X-ray structure determination was performed by the staff of Molecular Structure Corporation, 3304 Longmire Drive, College Station, Texas 77840.

Supplementary Material.

Additional X-ray data not published here for thiocarbazonate esters **11Ef** and **11Zu** are available from the authors.