Cyclization of Isothiosemicarbazones. 6.[1] The Formation and Structures of *N*-Alkenyl-1,2,4-triazoles and Related Compounds

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Alkanophenone 4-[2,2-bis(ethoxycarbonyl)vinyl]-3-methylisothiosemicarbazones and ortho-substituted acetophenone 4-[2-cyano-2-(ethoxycarbonyl)vinyl]-3-methylisothiosemicarbazones cyclize to 1-aryl-1-[3-(methylthio)-1*H*-1,2,4-triazol-1-yl]alkenes in acetic acid in moderate to good yields with elimination of diethyl malonate and ethyl cyanoacetate, respectively. When geometrical isomerism is possible, the triazolylalkenes have the *E* configuration. Aldehyde 4-[2,2-bis(ethoxycarbonyl)vinyl]- or 4-[2-cyano-2-(ethoxycarbonyl)vinyl]-3-methylisothiosemicarbazones undergo cleavage in acid to alkyl- or aryl[3-(methylthio)-1*H*-1,2,4-triazol-1-yl]methanol *O*-acylates and the corresponding malonate or cyanoacetate ester. The yields of *O*-acylate range from good in aromatic to poor in aliphatic compounds. The proposed mechanism for this acid-catalyzed cleavage of 4-(substituted vinyl)-3-methylisothiosemicarbazones involves a resonance-stabilized iminium cation as a common intermediate.

In a study of the cyclization of 4-(substituted vinyl)-isothiosemicarbazones, it was reported that **5a** was converted to **6** in hot acetic acid and that equilibrium was established between isothiosemicarbazones **5** and bicyclic pyrimidines **6** in hot pyridine.[1,2] It was also suggested[1] that **5j** underwent unexpected cleavage in hot acetic acid into a cyanoacetate and an unidentified product. Further study revealed that the latter was phenyl(1,2,4-triazol-1-yl)methanol acetate (**10j**). It has also been found that **5a** underwent similar elimination of ethyl cyanoacetate to produce an 1-vinyl-1,2,4-triazole derivative **9a** in addition to **7** when the acetic acid temperature was raised to reflux.

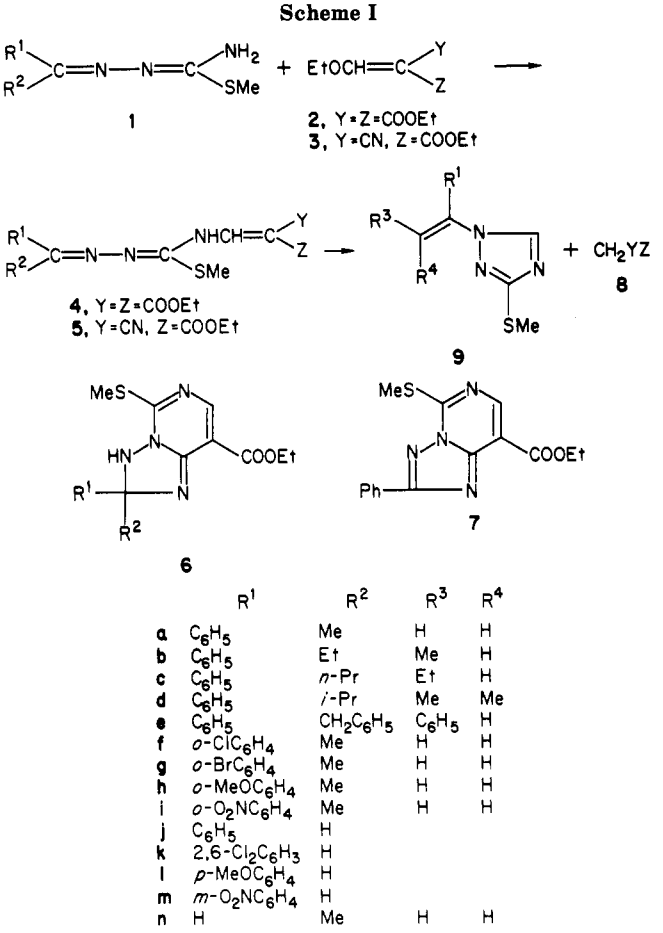
Only a few reports have been published in the past two decades on the synthesis of alkenyl azoles either by direct alkenylation[3] of the heterocycle or by modification[4] of substituents on the parent ring. To the best of our knowledge, nothing is known of simultaneous introduction of an alkenyl group in the course of the ring formation. Also unknown is an aryl(1,2,4-triazol-1-yl)methanol acylate (**10**), which can be considered to be an N-hemiacetal *O*-acylate formed formally by condensation of an aldehyde with a secondary amine.

The present paper describes a novel route to *N*-alkenyl-1,2,4-triazole derivatives and aryl(1,2,4-triazol-1-yl)-methanol *O*-acylates by the cyclization of 4-[2-cyano-2-(ethoxycarbonyl)vinyl]- and 4-[2,2-bis(ethoxycarbonyl)-vinyl]-3-methylisothiosemicarbazones in acidic media and a mechanism for the ring formation.

Results and Discussion

The formation of 2,2-disubstituted 2,3-dihydro[1,2,4]-triazolo[1,5-*c*]pyrimidines **6** requires a planar arrangement of nine atoms in the transition state and proceeds in an electrocyclic manner. Any factor that disrupts the coplanar geometry of the transition state should be unfavorable to or prevent the formation of **6**. To confirm this idea, 4-[2-cyano-2-(ethoxycarbonyl)vinyl]-3-methylisothiosemicarbazones **5f–i** of some ortho-substituted acetophenones were subjected to the optimal conditions for the preparation of **6a** from **5a**. The reaction of **5f–i** proceeded as expected in hot acetic acid to form **9** in low yields rather than **6** (Scheme I). The yields of **9f–h** were improved to 31–72% by conducting the reaction in refluxing acetic acid, the lowest yield being obtained with the *o*-nitro compound **9i**. This yield may reflect instability of the intermediate iminium ion **16** because of the electron-withdrawing NO_2 group.

Scheme I



	R^1	R^2	R^3	R^4
a	C_6H_5	Me	H	H
b	C_6H_5	Et	Me	H
c	C_6H_5	*n*-Pr	Et	H
d	C_6H_5	*i*-Pr	Me	Me
e	C_6H_5	$CH_2C_6H_5$	C_6H_5	H
f	*o*-ClC_6H_4	Me	H	H
g	*o*-BrC_6H_4	Me	H	H
h	*o*-$MeOC_6H_4$	Me	H	H
i	*o*-$O_2NC_6H_4$	Me	H	H
j	C_6H_5	H		
k	2,6-$Cl_2C_6H_3$	H		
l	*p*-$MeOC_6H_4$	H		
m	*m*-$O_2NC_6H_4$	H		
n	H	Me	H	H

The ortho substituent on R^1 of **5** favors the cyclization of **5** to form **9**. Thus, treatment of **5a** ($R^1 = C_6H_5$) in boiling acetic acid forms the dihydrotriazolopyrimidine **7** in addition to **9a**, whereas only **9** is formed from ortho-substituted **5**. Thus a general synthesis of **9** from **5** does not appear practical because of participation of the cyano group leading to the formation of triazolopyrimidines. However, the cyano group in **5** could be replaced by other sufficiently electron-withdrawing substituents capable of stabilizing a carbanion. Consequently, bis(ethoxy-

(1) Part 5: Yamazaki, C. *J Org. Chem.* **1981**, *46*, 3956.
(2) Yamazaki, C. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1767.
(3) (a) Fujiwara, Y.; Maruyama, O.; Yoshidomi, M.; Taniguchi, H. *J. Org. Chem.* **1981**, *46*, 851. (b) Taylor, E. C.; Martin, S. F. *J. Am. Chem. Soc.* **1974**, *96*, 8095.
(4) (a) Trofimenko, S. *J. Org. Chem.* **1970**, *35*, 3459. (b) Funaki, Y.; Ishiguri, Y.; Kato, T.; Tanaka, S. *J. Pesticide Sci.* **1984**, *9*, 229. (c) Yokoyama, M.; Tsuji, K.; Imamoto, T. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2954.

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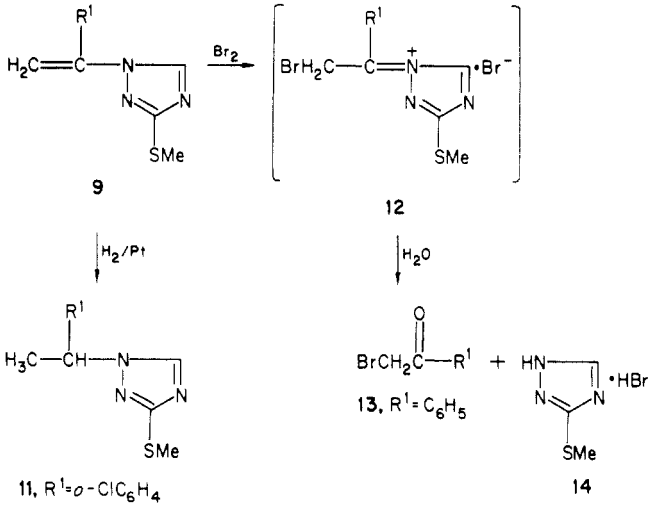
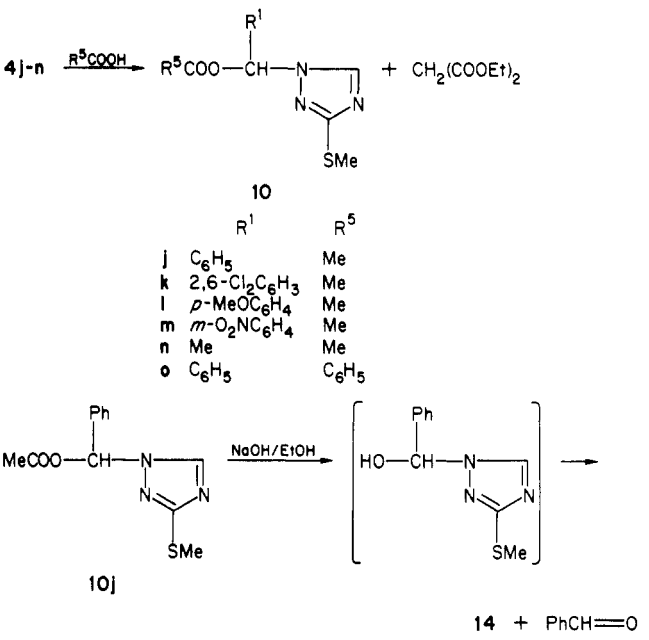
Scheme II



Scheme III



carbonyl)vinyl analogues **4a–e** were treated with hot acetic acid, and the reaction mixture was found to consist of **9** (yields 59–82%) and diethyl malonate (Scheme I). In contrast to the aromatic series, the aliphatic aldehyde isothiosemicarbazone **4n** did not form **9n** but produced only 8 in quantitative yield. The vinyltriazole **9n** was formed in 2% yield when **4n** was treated with trichloroacetic acid in boiling toluene.

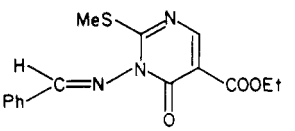
The terminal methylene structure of **9** was supported by the appearance of a triplet [δ 106.0–107.0 ($^1J_{CH}$ = 163–164 Hz)] in the vinylic region of the ^{13}C NMR spectrum. In the ^1H NMR spectrum, further support was obtained from the observation that the vinylic protons appeared as doublets at δ 5.05–6.04 with small coupling constants (0.3–1.5 Hz) due to geminal coupling. Upon hydrogenating over platinum, the vinylic carbon resonances of **9f** disappeared, and signals from a methyl carbon [δ 20.18 (q, $^1J_{CH}$ = 130 Hz)] and a methine carbon [δ 56.13 (d, $^1J_{CH}$ = 143 Hz)] were observed in the ^{13}C NMR spectrum of the product **11**. Further, appropriate resonances of the newly formed methyl [δ 1.89 (d, J = 7.0 Hz)] and methine protons [δ 5.95 (q, J = 7.0 Hz)] were observed in the ^1H NMR spectrum of **11**. Bromination of **9a** led to phenacyl bromide (**13**)[5] and 3-(methylthio)-1*H*-1,2,4-triazole (**14**) hydrobromide. The formation of these products may be explained by decomposition of the intermediate iminium salt **12** (Scheme II) and supports both the structure assignment of **9** and the enamine structure with the phenylvinyl moiety linked to the nitrogen of the triazole ring.

Treatment of benzaldehyde 4-[2-cyano-2-(ethoxycarbonyl)vinyl]-3-methylisothiosemicarbazone (**5j**) with hot acetic acid brought about cleavage to phenyl(1,2,4-triazol-1-yl)methanol *O*-acetate (**10j**) and 8 (Y = CN, Z = COOEt). Attempts to prepare **10** from the respective aldehyde and **14** in refluxing acetic acid were unsuccessful.

The 4-[2,2-bis(ethoxycarbonyl)vinyl]-3-methylisothiosemicarbazones **4** underwent similar cleavage in hot acetic acid to give **10** in higher yields (66–84%) than those from **5**. Steric and electronic factors appear to have no influence on the cleavage as shown by the nature of R^1 in Scheme III. The aliphatic vinyl isothiosemicarbazone **4n** gave **10n** in 35% yield. Substitution of benzoic acid for acetic acid in the reaction of **4j** gave the corresponding carbinol benzoate **10o**. On the other hand, treatment of **4j** with formic acid did not give the corresponding formate but rather **14** and 8 (Y = Z = COOEt).

Triazolylmethanol acylates **10** were characterized by the strong IR carbonyl bands at 1753–1766 (for acetates) and 1732 cm^{-1} (for benzoate) and by the resonance of the 1,2,4-triazole ring carbon at C-5, which appeared as a double doublet near δ 144 with a large coupling constant ($^1J_{CH}$ = 212 Hz), with each component splitting into a doublet ($^3J_{CH}$ = 2.7 Hz) due to long-range coupling with the hydrogen on the carbinol carbon. Hydrolysis of phenyl(1,2,4-triazol-1-yl)methanol acetate (**10j**) in dilute ethanolic sodium hydroxide at room temperature gave benzaldehyde and **14**, supporting the *O*-acetyl carbinolamine structure.

The formation of 1,2,4-triazoles from aldehyde or ketone 4-[2-cyano-2-(ethoxycarbonyl)vinyl]- or 4-[2,2-bis(ethoxycarbonyl)vinyl]-3-methylisothiosemicarbazones in acidic media with elimination of 8 could be explained by the mechanism shown in Scheme IV. For example, ring closure should occur through Michael-type addition of N-1 to the electron-deficient ethylenic linkage of the protonated species **15**. Abstraction of a proton by the carbanion C^-HYZ gives a resonance-stabilized iminium ion **16**. Reaction of **16** with a carboxylate anion produces carbinol acylate **10**. On the other hand, loss of a proton from the α carbon of iminium ion **16** would give the alkenyltriazoles **9**. Protonation of vinyl isothiosemicarbazones **4** and **5** may be essential for the ring closure. In fact, a basic medium such as pyridine or EtOH/sodium acetate has been found to promote alternative reaction pathways. For example, **5j** yields **7** as the only cyclized product in pyridine,[1] while its bis(ethoxycarbonyl) counterpart **4j** gives ethyl 1-(benzylideneamino)-1,6-dihydro-2-(methylthio)-6-oxopyrimidine-5-carboxylate (**17**) in EtOH/sodium acetate.



Experimental Section

Melting points were taken in open glass capillaries and are uncorrected. IR spectra were recorded in CCl_4 on a Perkin-Elmer

(5) Halogenation of enamines provides a synthesis of α-halo ketones, see: Carlson, R.; Rappe, C. *Acta Chem. Scand., Ser. B.* **1977**, *B31*, 485 and references cited therein.

Table I. Melting Points and Yields of 1, 4, and 5

			1		4		5	
	R^1	R^2	mp, °C	yield, %	mp, °C	yield, %	mp, °C	yield, %
a	C_6H_5	Me			102.5–103	88		
b	C_6H_5	Et	160–161[a]	76	71–72.5	80		
c	C_6H_5	*n*-Pr	194.5–195[a]	89	83.5–85[b]	51		
d	C_6H_5	*i*-Pr	101–103	93	56–58	59		
e	C_6H_5	$CH_2C_6H_5$	103–103.5	83	128–128.5	53		
f	*o*-ClC_6H_4	Me	58–60[c]	49				
f	*o*-ClC_6H_4	Me	124–125[d]	10			102–106[e]	42
g	*o*-BrC_6H_4	Me	61–63[c]	31				
g	*o*-BrC_6H_4	Me	118–120[d]	7			101–103[e]	60
h	*o*-$MeOC_6H_4$	Me	78–80	56			90–92[e]	56
i	*o*-$O_2NC_6H_4$	Me	103–105	40			126–127[e]	56
j	C_6H_5	H						
k	2,6-$Cl_2C_6H_3$	H						
l	*p*-$MeOC_6H_4$	H			105.5–106.5	73		
m	*m*-$O_2NC_6H_4$	H			149–150	43		
n	H	Me	79–80	66	68–71	95		

[a] Hydrochloride. [b] This compound contained a small amount of the *Z,E* isomer. [c] *E,E* isomer. [d] *E,Z* isomer. [e] *E,Z,E* isomer.

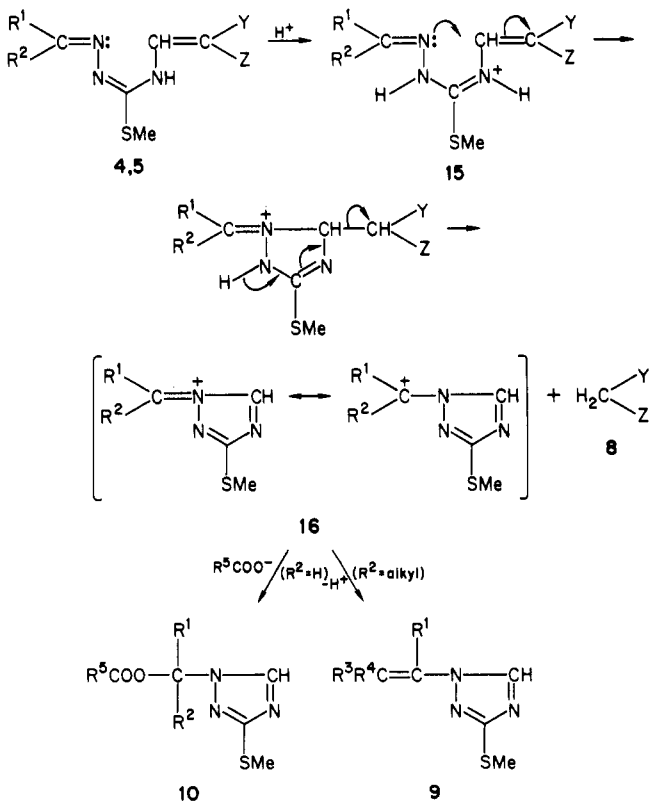
Table II. 1-[3-(Methylthio)-1*H*-1,2,4-triazol-1-yl)-1-arylethenes 9

	mp, °C	yield, %	^{1}H NMR, δ
a	oil	82	2.64 (3 H, s, SCH_3), 5.27 and 5.71 (1 H, d, *J* = 0.8 Hz, $=CH_2$),[9] 7.42 (5 H, s, C_6H_5), 8.00 (1 H, s, H-5 of triazole)
b	oil	59	1.77 (3 H, d, *J* = 7.3 Hz, $=CHCH_3$), 2.62 (3 H, s, SCH_3), 6.43 (1 H, q, *J* = 7.3 Hz, $=CHCH_3$), 7.23–7.52 (5 H, m, C_6H_5), 7.70 (1 H, s, H-5 of triazole)
c	oil	59	1.06 (3 H, t, *J* = 7.1 Hz, CH_2CH_3), 2.12 (2 H, quint, *J* = 7.6 Hz, CH_2CH_3), 2.63 (3 H, s, SCH_3), 6.37 (1 H, t, *J* = 7.9 Hz, $=CHCH_2$), 7.23–7.50 (5 H, m, C_6H_5), 7.69 (1 H, s, H-5 of triazole)
d[10]	oil	69	1.78 (3 H, s, $=CMeCH_3$), 1.94 (3 H, s, $=CCH_3Me$), 2.60 (3 H, s, SCH_3), 7.24–7.32 (5 H, m, C_6H_5), 7.94 (1 H, s, H-5 of triazole)
e	103–104	65	2.66 (3 H, s, SCH_3), 6.94–7.51 (10 H, m, C_6H_5), 7.36 (1 H, s, =CHPh), 7.74 (1 H, s, H-5 of triazole)
f	63–65	52	2.63 (3 H, s, SCH_3), 5.07 and 6.04 (1 H, d, *J* = 0.9 Hz, $=CH_2$), 7.41–7.46 (4 H, m, *o*-ClC_6H_4), 7.69 (1 H, s, H-5 of triazole)
g	oil	72	2.64 (3 H, s, SCH_3), 5.05 and 6.03 (1 H, d, *J* = 0.9 Hz, $=CH_2$), 7.33–7.73 (4 H, m, *o*-BrC_6H_4), 7.66 (1 H, s, H-5 of triazole)
h	70–71	57	2.64 (3 H, s, SCH_3), 3.73 (3 H, s, OCH_3), 5.05 and 5.95 (1 H, d, *J* = 0.3 Hz, $=CH_2$), 6.91–7.55 (4 H, m, *o*-$CH_3OC_6H_4$), 7.72 (1 H, s, H-5 of triazole)
i	95–96	31	2.56 (3 H, s, SCH_3), 5.11 and 5.86 (1 H, d, *J* = 1.5 Hz, $=CH_2$), 7.51–8.15 (4 H, m, *o*-$O_2NC_6H_4$), 7.98 (1 H, s, H-5 of triazole)
n	oil	2	2.62 (3 H, s, SCH_3), 5.02 (1 H, dd, ^2J = 1.2 Hz, ^3J = 8.8 Hz, vinyl proton trans to triazole ring), 5.74 (1 H, dd, ^2J = 1.2 Hz, ^3J = 15.4 Hz, vinyl proton cis to triazole ring), 6.98 (1 H, dd, ^3J = 8.8 and 15.4 Hz, vinyl proton geminal to triazole ring), 8.11 (1 H, s, H-5 of triazole)

983 spectrophotometer in a 1.0-mm KRS-5 cell. ^{1}H and ^{13}C NMR spectra were obtained with a JEOL FX 90Q spectrometer at 89.55 and 22.50 MHz, respectively. Chemical shifts are reported in δ downfield from internal Me_4Si in $CDCl_3$. Mass spectra (75 eV) were recorded on a JMS-D-100 mass spectrometer. UV spectra were recorded in EtOH on a JASCO UVIDEC 610 double-beam spectrophotometer. Preparative HPLC was carried out on a Kusano Kagaku KHLC-201 instrument using a 300 × 22 mm or a 300 × 10 mm glass column packed with silica gel. Satisfactory elemental analyses (±0.3% for C, H, and N) were obtained for all new compounds.

***E,E* 4-Unsubstituted Isothiosemicarbazones.**[6] Isothiosemicarbazones **1b–i** were prepared by refluxing the carbonyl compounds and *S*-methylisothiosemicarbazide hydriodide in EtOH acidified with concentrated HCl, evaporating the solvent under reduced pressure, washing the residue with $(i\text{-Pr})_2O$ to remove carbonyl compound, and decomposing the crude hydriodide with aqueous sodium carbonate. The crude **1f** and **1g** were contaminated with minor amounts of the *E,Z* isomer, which was removed by converting the mixtures into HCl salts and recrys-

Scheme IV



(6) A large steric compression shift (Wehrli, F. W.; Wirthlin, T. "Interpretation of Carbon-13 NMR Spectra"; Heyden & Son Inc.: London, 1978; p 187) was observed for two methyl carbons of the isopropylidene moiety of acetone *S*-methylisothiosemicarbazone (δ 17.91 and 25.09). The α-methyl carbon resonances of **1a,f–i** are in the range of δ 14.57–18.55, and two isomers isolated from crude **1f** and **1g** have resonances at δ 23.87 and 23.94, respectively. The isomeric form having the α-methyl carbon with upfield resonances should possess the *E,E* configuration (Hawkes, G. E.; Herwig, K.; Roberts, J. D. *J. Org. Chem.* **1974**, *39*, 1017). The stereochemistry about the N^2=C double bond of 4-unsubstituted isothiosemicarbazones was determined by the method reported previously.[7]

Table III. Aryl(1*H*-1,2,4-triazol-1-yl)methanol Acylates 10

	mp, °C	yield, %	^{1}H NMR, δ
j	63–65	77	2.20 (3 H, s, $COCH_3$), 2.57 (3 H, s, SCH_3), 7.45 (5 H, s, C_6H_5), 7.67 (1 H, s, CHO_2C), 8.07 (1 H, s, H-5 of triazole)
k	87.5–89	76	2.22 (3 H, s, $COCH_3$), 2.57 (3 H, s, SCH_3), 7.38 (3 H, m, 2,6-$Cl_2C_6H_3$), 8.15 (1 H, s, CHO_2C), 8.26 (1 H, s, H-5 of triazole)
l	glass	66	2.18 (3 H, s, $COCH_3$), 2.57 (3 H, s, SCH_3), 3.83 (3 H, s, OCH_3), 6.95 and 7.45 (2 H, d, J = 9 Hz, p-$CH_3OC_6H_4$), 7.61 (1 H, s, CHO_2C), 8.04 (1 H, s, H-5 of triazole)
m	88–90	84	2.25 (3 H, s, $COCH_3$), 2.55 (3 H, s, SCH_3, 7.54–8.44 (4 H, m, m-$O_2NC_6H_4$), 7.70 (1 H, s, CHO_2C), 8.28 (1 H, s, H-5 of triazole)
n	glass	35	1.85 (3 H, d, J = 6.3 Hz, $CHCH_3$), 2.07 (3 H, s, $COCH_3$), 2.60 (3 H, s, SCH_3), 6.74 (1 H, q, J = 6.3 Hz, $CHCH_3$), 8.23 (1 H, s, H-5 of triazole)
o	74.5–76.5	36	2.57 (3 H, s, SCH_3), 7.28–7.62 (8 H, m, C_6H_5), 7.93 (1 H, s, CHO_2C), 8.02–8.16 (2 H, m, C_6H_5), 8.18 (1 H, s, H-5 of triazole)

tallizing the salts from EtOH. Compound **1n** was obtained by reacting a 20% molar excess of 90% aqueous acetaldehyde with *S*-methylisothiosemicarbazide hydriodide formed in situ from an equimolar mixture of thiosemicarbazide and CH_3I in warm MeOH. Other isothiosemicarbazones were obtained according to the literature.[7] Melting points and yields are given in Table I.

4-[2,2-Bis(ethoxycarbonyl)vinyl]-3-methylisothiosemicarbazones 4a–e,j–n and 4-[2-cyano-2-(ethoxycarbonyl)vinyl]-3-methylisothiosemicarbazones 5f–i were prepared according to the literature.[8] Compound **4n** was best prepared by heating **1n** with **2** in benzene containing Et_3N for 6 h. Melting points and yields are given in Table I.

1-[3-(Methylthio)-1,2,4-triazol-1-yl]-1-phenylethene (9a) (General Procedure for Cyclizing 4a–e). A solution of **4a** (1.0 g) in acetic acid (4 mL) was heated at 90 °C for 1.5 h and evaporated under reduced pressure. The residue was shaken thoroughly with 25% aqueous NaOH (15 mL) to remove diethyl malonate. The dispersed oil was extracted 2× with $CHCl_3$, and the combined organic layers were washed with 25% NaOH and water and dried over Na_2SO_4. After evaporation of the solvent, crude **9a** was purified by column chromatography on silica gel, eluting with $CHCl_3$. Properties and yields of **9** are given in Table II. Refluxing **4a** in formic acid for 2.5 h and workup gave **9a** in lower (43%) yield. In addition, heating **5a** in boiling acetic acid gave **9a** (15%) along with **7** (12%).

3-(Methylthio)-1-vinyl-1*H*-1,2,4-triazole (9n). A mixture of **4n** (5.0 g), Cl_3CCO_2H (1.0 g), and toluene (20 mL) was refluxed for 30 min and worked up as above. Repeated HPLC (silica gel, 1:1 v/v $CHCl_3$–CH_2Cl_2) gave 0.06 g (2%) of **9n**.

Phenyl(1,2,4-triazol-1-yl)methanol Acetate (10j) (General Procedure for Cyclizing 4j–o). A mixture of **4j** (0.5 g) and acetic acid (2 mL) was heated at 90 °C for 1.5 h and then evaporated under reduced pressure. The residue was dissolved in $CHCl_3$, washed with Na_2CO_3 solution and water, and dried (Na_2SO_4). After removal of the solvent, the residue was subjected to HPLC over silica gel, eluting with $CHCl_3$, to give **10j** as a colorless oil (0.28 g, 77%), which crystallized after standing 10 days. Properties of **10j–n** are given in Table III.

Phenyl(1,2,4-triazol-1-yl)methanol Benzoate (10o). A mixture of **4j** (0.5 g, 13.8 mmol), benzoic acid (2.0 g, 164 mmol), and toluene (2 mL) was heated at 90 °C for 1.5 h and then diluted with benzene (10 mL). The solution was washed with 5% $NaHCO_3$ and then repeatedly with water, dried over Na_2SO_4, and evaporated under reduced pressure. The residue (0.3 g) was subjected to preparative HPLC over silica gel, eluting with CH_2Cl_2, to give **10o** as a colorless oil (0.16 g, 36%, Table III).

Bromination of 9a. To an ice-cooled, stirred solution of **9a** (0.1 g, 0.46 mmol) in CCl_4 (1 mL) was added dropwise a solution of Br_2 (0.08 g, 0.5 mmol) in CCl_4. The red color disappeared rapidly, and a cloudy solution resulted. After the solvent was evaporated, the remaining orange powder was triturated with EtOH and collected by filtration to give a white powder (0.08 g) that was identified as **14** hydrobromide by its IR spectrum and by mixed melting point with an authentic sample (mp 185–187 °C). The filtrate was concentrated to a small volume and allowed to crystallize to afford irritating crystals (0.05 g), identified as phenacyl bromide (**13**, $R^1 = C_6H_5$) by IR and ^{1}H NMR spectra.

1-(*o*-Chlorophenyl)-1-[3-(methylthio)-1,2,4-triazol-1-yl]-ethane (11). A mixture of **9f** (0.3 g), platinum oxide (0.15 g), and MeOH (6 mL) was stirred under hydrogen at room temperature and atmospheric pressure. The reaction was followed by ^{1}H NMR measurements of periodic aliquots. After 10 days, the reaction was 70% complete and was discontinued. The reaction mixture was passed through a small column packed with silica gel (5 g) to remove the catalyst and evaporated. The crude **11** was isolated from the residue by HPLC on silica gel, eluting with CH_2Cl_2, as a colorless oil (0.093 g, 35%): ^{1}H NMR δ 1.89 (3 H, d, J = 7.0 Hz, $CHCH_3$), 2.59 (3 H, s, SCH_3) 5.95 (1 H, q, J = 7.0 Hz, $CHCH_3$), 7.24–7.44 (4 H, m, o-ClC_6H_4), 8.02 (1 H, s, H-5 of triazole); perchlorate mp 51–53 °C.

Hydrolysis of 10j. A solution of **10j** (0.4 g) in 1% ethanolic NaOH (2 mL) was allowed to stand at room temperature for 30 min. After neutralization with aqueous acetic acid, the mixture was evaporated at 40 °C (bath temperature) under reduced pressure and the residue extracted with benzene. The benzene-insoluble fraction afforded **14** (0.09 g) as white crystals, mp 101 °C, and not depressed on admixture with an authentic sample.[11] The benzene extract afforded benzaldehyde (0.08 g).

Ethyl 1-(Benzylideneamino)-1,6-dihydro-2-(methylthio)-6-oxo-5-pyrimidinecarboxylate (17). A mixture of **4j** (2.0 g) and NaOAc (5.0 g) in EtOH (50 mL) was refluxed for 2 h and the solvent then removed by evaporation under reduced pressure. The residue was triturated with $CHCl_3$ (20 mL) to extract **17**. After evaporation of the $CHCl_3$ the remaining white solid was recrystallized from MeOH to give **17** (1.2 g, 68%): mp 136–137 °C; ^{1}H NMR δ 1.38 (3 H, t, J = 7 Hz, OCH_2CH_3), 2.55 (3 H, s, SCH_3), 4.38 (2 H, q, J = 7 Hz, OCH_2CH_3), 7.53 (3 H, m, C_6H_5), 7.88 (2 H, m, C_6H_5), 8.54 (1 H, s, H-4 of dihydropyrimidine ring), 9.19 (1 H, s, N=CH).

Supplementary Material Available: ^{1}H NMR data peaks of **4a–e,l–n** and **5f–i** and ^{13}C NMR and UV data peaks of **9a–i,n**, **10j–o**, **11**, and **17** (8 pages). Ordering information is given on any current masthead page.

(7) Yamazaki, C. *Can. J. Chem.* **1975**, *53*, 610.
(8) Yamazaki, C. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1767.
(9) Assignment of the vinylic proton resonances can be made with reference to those of 1-vinyl-3-methylthio-1*H*-1,2,4-triazole (**9n**), in which the three vinylic hydrogens appear at δ 5.02, 5.74, and 6.98 and are assigned to the trans, cis, and *gem* hydrogens, respectively, on the basis of their coupling constants (J_{cis} = 8.7, J_{trans} = 15.5, and J_{gem} = 1.2 Hz). The (methylthio)-1*H*-1,2,4-triazolyl group causes a very large (−1.73 ppm) downfield shift for a vinylic proton from the *gem* position and a moderate (−0.49 ppm) downfield shift from the cis position but a small (+0.23 ppm) upfield shift from the trans position. Thus the chemical shifts of the two vinylic protons of styryltriazoles can be calculated by the combination of increments of two aromatic rings on the ethylenic carbon. The observed values, δ 5.27 and 5.71 in **9a**, are very close to the predicted values, δ 5.38 and 5.67, using the shielding constants of the phenyl group, δ −0.38 for the cis and δ 0.0 for the trans proton. The upfield resonances in a given pair of vinylic protons can generally be assigned to the proton trans to the triazolyl and cis to the aryl groups. Taking into account the strong similarity of their UV spectra, the ortho substituents would not influence the steric environment of the two aromatic rings such that this prediction is invalidated.
(10) The starting **4d** was less reactive and required more vigorous conditions, i.e., refluxing for 3 h, to achieve the indicated yield. In the IR spectrum of **9d**, the $\nu_{C=C}$ band was not seen in the usual region.
(11) Kroeger, C. F.; Sattler, W.; Beyer, H. *Ann.* **1961**, *643*, 128.