CH_2Br, CH_3, H, 6-Cl, 19359-33-2; **2**, C_6H_5, Cl, H, 6-Cl, 17259-82-4; **2**, C_6H_5, Cl, H, 6-CH_3, 19398-22-2; **2**, C_6H_5, Cl, C_2H_5H, 19359-35-4; **2**, C_6H_5, H, C_2H_5, 6-Cl, 19359-36-5; **3c**, 19359-37-6; **3d**, 19359-38-7; **3e**, 19375-64-5; **3f**, 19359-39-8; **3g**, 19359-40-1; **3h**, 19359-41-2; **3i**, 19359-42-3; **3j**, 19359-43-4; **3k**, 19359-44-5; **4b**, 19359-45-6; **4c**, 19359-46-7; **4d**, 19359-47-8; **4d** O-acetate, 19359-48-9; **4d** O-benzoate, 19359-49-0; **5**, 19359-50-3; **6**, 19359-51-4; **7**, 19359-52-5; **8a**, 19359-53-6; **8b**, 19359-54-7.

Synthesis and Cyclizations of Semicarbazidomethylenemalonates and Related Compounds

ROBERT K. HOWE AND SUSAN C. BOLLUYT

Monsanto Company, Agricultural Division, Research Department, St. Louis, Missouri 63166

Received October 18, 1968

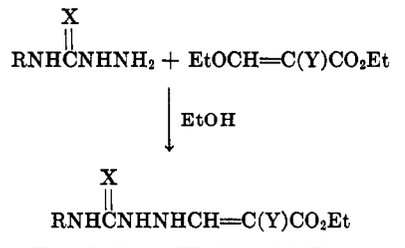
Reaction of semicarbazides and thiosemicarbazides with diethyl ethoxymethylenemalonate produced **1a–c** and **2a–c** in high yields. Use of ethyl 2-cyano-3-ethoxyacrylate led to **3a–c** and **4a–c**. Reaction of semicarbazides with ethoxymethylenemalononitrile (EMMN) produced **5a** and **b** and **6a** and **b**. Thiosemicarbazides and EMMN produced **7a** and **b**. Attempts to cyclize **1a** and **b** in hot ethanol were unsuccessful. Cyclization of **2a** and **2c** in hot ethanol gave 2-(ethylamino)- and 2-(anilino)-1,3,4-thiadiazole, respectively. Cyclization of **3a** gave **8a**, and **3b** gave **8b**, which readily lost the 1-phenylcarbamoyl group through solvolysis. Compound **4a** gave **9** upon cyclization, and **4c** gave ethyl 5-amino-4-pyrazolecarboxylate.

Hydrazinomethylenemalonates[1] and 3-hydrazino- and 3-(acylhydrazino)-2-cyanoacrylates[2,3] have been reported, and their cyclizations to pyrazole derivatives have been studied.[1–3] Hydrazines react with ethoxymethylenemalononitrile to produce pyrazoles *via* intermediate hydrazinomethylenemalononitriles which generally were not isolable.[4] Diethyl semicarbazidomethylenemalonate and diethyl thiosemicarbazidomethylenemalonate have been reported.[5] The reaction of semicarbazide with ethoxymethylenemalononitrile has been reported to give semicarbazidomethylenemalononitrile[6,7] under mild reaction conditions and 5-amino-4-cyano-1-pyrazolecarboxamide[8] under more vigorous reaction conditions.

We have studied the reactions of 4-substituted semicarbazides and 4-substituted 3-thiosemicarbazides with diethyl ethoxymethylenemalonate, ethyl 2-cyano-3-ethoxyacrylate, and ethoxymethylenemalononitrile. Reactions of semicarbazides and thiosemicarbazides with diethyl ethoxymethylenemalonate in ethanol at 20–25° gave semicarbazido- and thiosemicarbazidomethylenemalonates **1a–c** and **2a–c**, and use of ethyl 2-cyano-3-ethoxyacrylate in this condensation reaction gave **3a–c** and **4a–c** (Scheme I, Table I).

The reaction of semicarbazide with ethoxymethylenemalononitrile (EMMN) was reinvestigated; that semicarbazidomethylenemalononitrile[6,7] (**5a**) is obtained under mild reaction conditions was verified through

SCHEME I

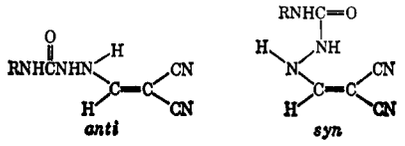


1a, X = O; R = CH_3; Y = CO_2Et
b, X = O; R = C_6H_5; Y = CO_2Et
c, X = O; R = 3,4-$Cl_2C_6H_3$; Y = CO_2Et
2a, X = S; R = Et; Y = CO_2Et
b, X = S; R = allyl; Y = CO_2Et
c, X = S; R = C_6H_5; Y = CO_2Et
3a, X = O; R = CH_3; Y = CN
b, X = O; R = C_6H_5; Y = CN
c, X = O; R = 3,4-$Cl_2C_6H_3$; Y = CN
4a, X = S; R = Et; Y = CN
b, X = S; R = allyl; Y = CN
c, X = S; R = C_6H_5; Y = CN

nmr analysis of the product.[9] Reaction of 4-methylsemicarbazide with ethoxymethylenemalononitrile (EMMN) in ethanol at 23° led to (4-methylsemicarbazido)methylenemalononitrile[9] (**5b**) in 52% yield

(1) L. Claisen and E. Haase, *Chem. Ber.*, **28**, 35 (1895).
(2) P. Schmidt and J. Druey, *Helv. Chim. Acta*, **39**, 986 (1956).
(3) P. Schmidt, K. Eichenberger, and J. Druey, *ibid.*, **41**, 1052 (1958).
(4) C. C. Cheng and R. K. Robins, *J. Org. Chem.*, **21**, 1240 (1956).
(5) A. A. Santilli, W. F. Bruce, and T. S. Osdene, *J. Med. Chem.*, **7**, 68 (1964).
(6) M. J. Kamlet, *J. Org. Chem.*, **24**, 714 (1959).
(7) C. Runti, L. Sindellari, and C. Nisi, *Ann. Chim.* (Rome), **49**, 1649 (1959).
(8) C. L. Dickinson, J. K. Williams, and B. C. McKusick, *J. Org. Chem.*, **29**, 1915 (1964).

(9) The nmr spectra of **5a** and **5b** reveal hindered rotation about the vinyl carbon–nitrogen bond, with unequal populations of the *anti* and *syn* conformers; the vinyl proton and the adjacent NH proton each appear as two singlets of unequal intensity. Similarly, *anti–syn* isomerism has been observed with N-alkylaminomethylenemalononitriles (R. K. Howe, unpublished work),



and hindered rotation about the vinyl carbon–nitrogen bond of N,N-dimethylaminomethylenemalononitrile has been reported by A. Mannschreck and U. Koelle [*Tetrahedron Lett.*, 863 (1967)].

TABLE I

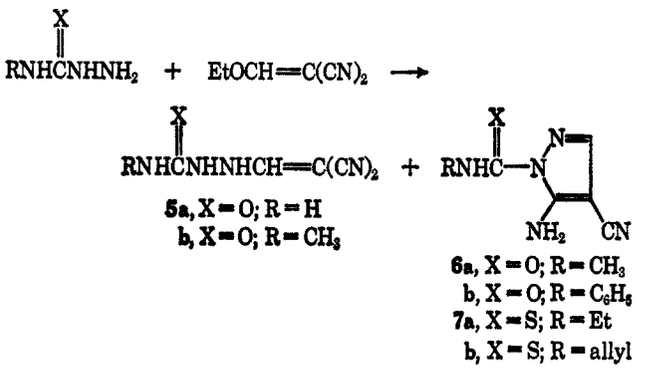
SEMICARBAZIDO- AND THIOSEMICARBAZIDOMETHYLENEMALONATES, AND SEMICARBAZIDO- AND THIOSEMICARBAZIDO-2-CYANOACRYLATES

Compd	Mp, °C	Yield, %	Formula	Calcd, %			Found, %			Ir spectra		
				C	H	N	C	H	N	NH	C=O	CN
1a	190–192	97[a]	$C_{10}H_{17}N_3O_5$	46.33	6.61	16.21	46.51	6.72	16.18	3.00, 3.10	5.89, 6.01	
1b	161–162	95	$C_{15}H_{19}N_3O_5$	56.07	5.96	13.08	56.11	5.79	13.01	3.00, 3.10	5.85 sh, 5.95, 6.10	
1c	178–180	96	$C_{15}H_{17}Cl_2N_3O_5$	46.17	4.39	10.77	45.88	4.44	10.64	3.05, 3.15	5.85, 5.95, 6.01	
2a	160–162	84	$C_{11}H_{19}N_3O_4S$	45.66	6.62	14.52	45.81	6.80	14.57	3.08, 3.24	5.87, 6.04	
2b	151–153	66	$C_{12}H_{19}N_3O_4S$	47.83	6.35	13.94	47.62	6.45	13.81	3.08, 3.22	5.84, 6.05	
2c	129–131	74[b]	$C_{15}H_{19}N_3O_4S$	53.40	5.68	12.45	53.47	5.73	12.56	3.10, 3.20	5.85, 6.03	
3a	180–181	85[a]	$C_9H_{12}N_4O_3$	45.28	5.70	26.40	45.47	5.55	26.57	3.02, 3.10	5.85 sh, 5.95, 6.01	4.51
3b	158–161	85	$C_{13}H_{14}N_4O_3$	56.93	5.15	20.43	56.73	5.12	20.25	3.07	5.85 sh, 5.97	4.51
3c	161–163	72	$C_{13}H_{12}Cl_2N_4O_3$	45.50	3.52	16.33	45.63	3.57	16.14	3.00, 3.08	5.85 sh, 5.91, 6.05	4.51
4a	141–142	90	$C_9H_{14}N_4O_2S$	44.61	5.82	23.12	44.59	5.99	23.01	3.02, 3.20	5.85 sh, 5.92	4.51
4b	139–141	68	$C_{10}H_{14}N_4O_2S$	47.23	5.55	22.03	47.10	5.68	21.68	3.20	5.85, 5.90 sh	4.51
4c	137–138	28	$C_{13}H_{14}N_4O_2S$	53.78	4.86	19.30	54.04	4.91	19.14	3.20	5.85	4.51

[a] Reaction in 50% aqueous ethanol. [b] Reaction in ethanol–THF, and solution cooled on ice to precipitate product.

and also to **6a** in 25% yield (Scheme II). The solubility differences of **5b** and **6a** allowed isolation of each in pure form. Conversion of **5b** to **6a** occurred in 75% yield in ethanol at reflux for 2 hr. The reaction of 4-phenylsemicarbazide with EMMN in ethanol at 23° led to **6b** in 32% yield. Attempts to obtain pure noncyclized product in this case were unsuccessful. The reactions of 4-ethyl- and 4-allyl-3-thiosemicarbazides with EMMN led to **7a** and **7b** in good yields. That the products are ring closed is indicated by the recovery of **7a** unchanged from ethanol at reflux for

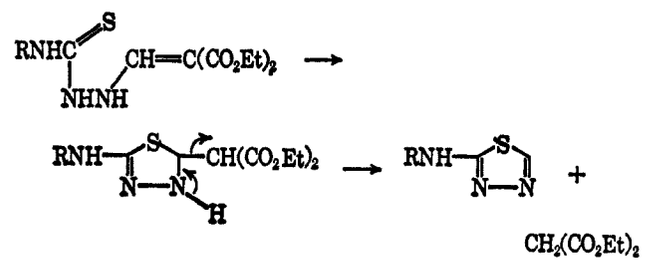
SCHEME II



4 hr and by the nmr spectrum of **7a** that shows one NH signal and one NH_2 singlet (in dimethyl sulfoxide-d_6). The intermediate thiosemicarbazidomethylenemalononitriles were not detected; cyclization of these derivatives apparently is extremely facile.

Attempted cyclization of **1a** in ethanol at reflux for 10 days led to 78% recovery of **1a**, while **1b** in ethanol at reflux for 4.6 days gave 1,6-diphenylbiurea, in 24% yield, through an undetermined pathway. Cyclization of **2a** and **2c** in hot ethanol was achieved; **2a** gave 2-ethylamino-1,3,4-thiadiazole (31% yield) and diethyl malonate (59%), and **2c** gave 2-anilino-1,3,4-thiadiazole (77%). This reaction (Scheme III) is quite similar to the preparation of 1,3,4-thiadiazoles from thiosemicarbazides and triethyl orthoformate reported by Whitehead and Traverso.[10]

SCHEME III

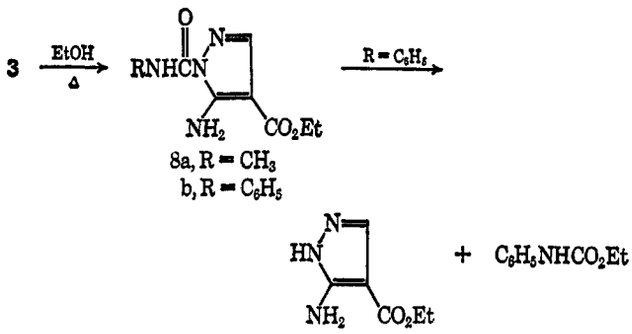


The major cyclization pathway taken by compounds **3** is the one leading to the 5-amino-1-carbamoyl-4-pyrazolecarboxylates (Scheme IV). In ethanol at reflux **3a** gave **8a** in 55% yield. Ethyl 5-amino-4-pyrazolecarboxylate was formed in 74% yield from **3b** in ethanol at reflux for 16 hr, *via* solvolysis of the

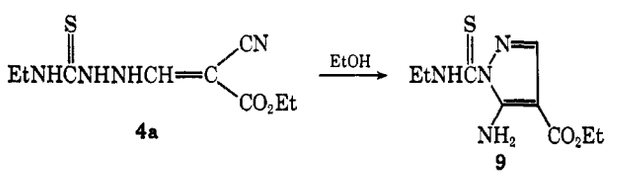
(10) C. W. Whitehead and J. J. Traverso, *J. Amer. Chem. Soc.*, **77**, 5872 (1955).

intermediate **8b**. A shorter reaction time allowed isolation of **8b** in 15% yield.

SCHEME IV



Thiosemicarbazido-2-cyanoacrylates cyclize to 5-amino-4-pyrazolecarboxylates. Cyclization of **4a** in ethanol gave **9** in 59% yield. In hot ethanol **4c**



produced a mixture that contained ethyl 5-amino-4-pyrazolecarboxylate (19%) and 1,6-diphenyl-2,5-dithiobiurea (14%). The phenylthiocarbamoyl group is also readily lost from the ring nitrogen atom of pyrazoles in hot ethanol. The available data do not allow a choice to be made among the numerous possibilities for pathways leading to the biurea.

The present work illustrates that compounds of the type **1–5** are readily obtainable under mild reaction conditions and outlines the major cyclization pathways taken by these compounds. The previous literature and the present results show that uncatalyzed intramolecular cyclization into the ester group of 3-hydrazinoacrylates is difficult. Cyclization of diethyl phenylhydrazinomethylenemalonate to ethyl 1-phenyl-5-pyrazolon-4-carboxylate required a temperature of *ca.* 170°.[1] Thus compounds of type **1** do not readily cyclize to pyrazoles, and compounds of type **2** cyclize through an alternative pathway to thiadiazoles. In contrast, cyclization into the cyano group of 3-hydrazinoacrylonitriles is a relatively easy process.[2,3] Semicarbazido- and thiosemicarbazido-2-cyanoacrylates, and semicarbazido- and thiosemicarbazidomethylenemalononitriles readily cyclize into the cyano group in hot ethanol to 5-aminopyrazole derivatives. The methylenemalononitriles cyclize easier than the 2-cyanoacrylates, as expected from the relative electron withdrawing effects of a cyano substituent and a carbethoxy substituent α to the cyano group that undergoes nucleophilic attack in the cyclization reaction.

Experimental Section[11]

General Procedure for Semicarbazidomethylene Compounds.—A solution of the semicarbazide or thiosemicarbazide and 1.05 equiv of diethyl ethoxymethylenemalonate, ethyl 2-cyano-3-ethoxyacrylate, or ethoxymethylenemalononitrile in ethanol is held overnight at 20–25°. The resultant solid is collected and washed with ethanol.

4-(3,4-Dichlorophenyl)semicarbazide.—A solution of 215 g (1.15 mol) of 3,4-dichlorophenyl isocyanate in 2 l. of ether was added slowly to 298 g (8 equiv) of hydrazine in ether with stirring and cooling. The temperature was maintained below 20°. After the addition was completed, the ether layer was decanted from an oily layer. Dilution of the oily layer with water produced a solid, which, after vacuum drying, weighed 237.5 g. This material was recrystallized from ethanol, with filtration to remove the insoluble 1,6-bis(3,4-dichlorophenyl)-biurea, to give 108.6 g of solid, mp 175–177°. This solid was recrystallized from 700 ml of ethyl acetate (filtration) to give 77.3 g (30%) of solid: mp 173–175°; ir 3.00, 3.10 (NH), 5.90 μ (C=O). *Anal.* Calcd for $C_7H_7Cl_2N_3O$: C, 38.20; H, 3.20; N, 19.09. Found: C, 38.38; H, 3.28; N, 18.99.

Diethyl [(4-methylsemicarbazido)methylene]malonate (1a) (see Table I) had nmr τ 0.27 (broad d, 1, J = 11 Hz, NHCH=C), 1.32 (bs, 1, NH), 2.25 (d, 1, J = 11 Hz, NHCH=C), 3.51 (b, 1, CH_3NH), 5.87 (q, 2, J = 7 Hz, OCH_2CH_3), 5.92 (q, 2, J = 7 Hz, OCH_2CH_3), 7.40 (d, 3, J = 4.5 Hz, CH_3NH), 8.78 (t, 6, J = 7 Hz, OCH_2CH_3).

Diethyl [(4-phenylsemicarbazido)methylene]malonate (1b) (see Table I) had nmr τ −0.05 (broad d, 1, J = 11 Hz, NHCH=C), 0.92 (s, 1, NH), 1.13 (s, 1, NH), 2.05 (d, 1, J = 11 Hz, NHCH=C), 2.3–3.1 (m, 5, C_6H_5), 5.83 (m, 4, OCH_2CH_3), 8.77 (t, 6, J = 7 Hz, OCH_2CH_3).

Ethyl 2-cyano-3-(4-methylsemicarbazido)acrylate (3a) (see Table I) had nmr τ −0.04 (bs, 1, NH), 1.38 (b, 1, NH), 2.21 (s, 1, CH=C), 3.53 (bm, 1, CH_3NH), 5.86 (q, 2, J = 7 Hz, OCH_2CH_3), 7.39 (d, 3, J = 4.5 Hz, CH_3NH), 8.79 (t, 3, J = 7 Hz, OCH_2CH_3).

Ethyl 2-cyano-3-(4-phenylsemicarbazido)acrylate (3b) (see Table I) had nmr τ −0.10 (bs, 1, NH), 1.14 (b, 2, NH), 2.12 (s, 1, CH=C), 2.35–3.15 (m, 5, C_6H_5), 5.85 (q, 2, J = 7 Hz, OCH_2CH_3), 8.78 (t, 3, J = 7 Hz, OCH_2CH_3).

Ethyl 2-Cyano-3-(4-phenyl-3-thiosemicarbazido)acrylate (4c).—A solution of 50 g (0.299 mol) of 4-phenyl-3-thiosemicarbazide and 52.4 g (1.05 equiv) of ethyl 2-cyano-3-ethoxyacrylate in ethanol–tetrahydrofuran was allowed to stand overnight. The resultant solid, 10.6 g (23%), mp 178–179° (lit.[12] mp 173°), was collected and identified as 1,6-diphenyl-2,5-dithiobiurea from the ir and nmr spectra.

Anal. Calcd for $C_{14}H_{14}N_4S_2$: C, 55.60; H, 4.67; N, 18.53; S, 21.20. Found: C, 55.73; H, 4.76; N, 18.49; S, 20.94.

Concentration of the filtrate gave 31.5 g of solid, mp 131–148°. The solid was dissolved in 600 ml of tetrahydrofuran at 35°, the solution was cooled on ice, and water was added to the cloud point. The resultant solid was collected and washed well with ethanol to give 23.9 g (28%) of **4c**: mp 137–138°, resolidified at 138° and remelted at 144–146° (see Table I).

Semicarbazidomethylenemalononitrile (5a).—To a solution of 11.1 g (0.10 mol) of semicarbazide hydrochloride in 75 ml of water was added 8.2 g (0.10 mol) of sodium acetate. To the resultant solution was added 12.2 g of ethoxymethylenemalononitrile in 175 ml of ethanol. The clear solution slowly deposited solid. After 1.5 hr, the solid was collected and washed with 35 ml of water. There resulted 5.5 g of solid, mp 169°, with melting and rapid resolidification: ir 2.9, 3.08 (NH), 4.51 (CN), 5.96 (C=O), 6.12 μ (amide II); nmr τ −0.40 (s, 1, NH), 1.28, 1.40 (singlets, 0.3 H and 0.7 H, NHCH=C), 2.03, 2.38 (singlets, 0.3 H and 0.7 H, NHCH=C), 3.83 (bs, 2, NH_2).

Anal. Calcd for $C_5H_5N_5O$: C, 39.74; H, 3.33; N, 46.34. Found: C, 39.60; H, 3.18; N, 46.18.

(4-Methylsemicarbazido)methylenemalononitrile (5b) and 5-Amino-4-cyano-N-methyl-1-pyrazolecarboxamide (6a).—A solution of 40 g (0.45 mol) of 4-methylsemicarbazide in 50% aqueous ethanol was added to 57.5 g (1.05 equiv) of ethoxymethylenemalononitrile in ethanol. The solution was allowed to stand overnight. The resultant solid, 3.7 g, mp 171–174°, was collected. The filtrate was concentrated under vacuum below 30° to give 38.8 g (52%) of **5b**: mp 148–150°; ir 3.00, 3.20 (NH), 4.51 (CN), 5.90 μ (C=O); nmr τ −0.53 (b, 1, NH), 1.17, 1.24 (singlets, 0.25 H and 0.75 H, NHCH), 1.93, 2.05 (singlets,

(11) Melting points were determined with a Mel-Temp apparatus in open capillary tubes and are corrected. Nmr spectra were determined on a Varian A-60 spectrometer with dimethyl sulfoxide-d_6 solvent and internal tetramethylsilane standard. Ir spectra were determined on the compounds in mineral oil mulls on a Beckman IR-5 spectrometer.

(12) S. L. Janniah and P. C. Guha, *J. Indian Inst. Sci.*, **16A**, 11 (1963); *Chem. Abstr.*, **27**, 3711 (1933).

0.25 H and 0.75 H, NHCH), 3.42 (m, 1, CH_3NH), 7.73 (d, 3, J = 4.5 Hz, CH_3NH).

Anal. Calcd for $C_6H_7N_5O$: C, 43.64; H, 4.27; N, 42.40. Found: C, 43.86; H, 4.36; N, 42.63.

The filtrate from **5b** after standing overnight gave 21.2 g of solid, mp 172–175°. This solid was combined with the 3.7 g of solid, mp 171–174°; 24.9 g of solid was dissolved in warm water, and the solution was cooled on ice to give 18.3 g (25%) of **6a**: mp 173–175°; ir 2.9–3.1 (NH), 4.51 (CN), 5.85 μ (C=O); nmr τ 1.72 (b, 1, CH_3NH), 2.16 (s, 1, CH=), 2.33 (b, 2, NH_2), 7.21 (d, 3, J = 5 Hz, CH_3NH).

Anal. Found: C, 43.43; H, 4.30; N, 42.15.

A 2-g sample of **5b** in ethanol was held 2 hr at reflux. Upon cooling the solution produced 1.5 g (75%) of **6a**, mp 175–177°, identified by ir and nmr spectra and by melting point.

5-Amino-4-cyano-N-phenyl-1-pyrazolecarboxamide (6b).—A solution of 25 g (0.165 mol) of 4-phenylsemicarbazide and 21.2 g (1.05 equiv) of ethoxymethylenemalononitrile in 450 ml of ethanol was allowed to stand overnight. The solution was concentrated. The solid residue was extracted with hot acetone, and the insoluble solid was removed by filtration. The filtrate was concentrated and cooled on ice to give 11.7 g (32%) of **6b**: mp 171–173°; ir 2.9–3.1 (NH), 4.51 (CN), 5.80 μ (C=O).

Anal. Calcd for $C_{11}H_9N_5O$: C, 58.14; H, 3.99; N, 30.82. Found: C, 58.32; H, 4.01; N, 30.89.

5-Amino-4-cyano-N-ethyl-1-pyrazolethiocarboxamide (7a).—A solution of 25 g (0.210 mol) of 4-ethyl-3-thiosemicarbazide and 26.8 g (1.05 equiv) of ethoxymethylenemalononitrile in ethanol was allowed to stand overnight. The resultant solid, mp 146–148°, weighed 33.4 g (81%): ir 3.06 (NH), 4.51 μ (CN); nmr τ −0.24 (bs, 1, NH), 1.30 (bs, 2, NH_2), 2.03 (s, 1, CH=), 6.33 (bq, 2, NCH_2CH_3), 8.79 (t, 3, NCH_2CH_3).

Anal. Calcd for $C_7H_9N_5S$: C, 43.06; H, 4.65; N, 35.87. Found: C, 43.18; H, 4.65; N, 35.92.

A sample of **7a** was recovered unchanged after 4 hr at reflux in ethanol.

N-Allyl-5-amino-4-cyano-1-pyrazolethiocarboxamide (7b).—A solution of 15 g (0.114 mol) of 4-allyl-3-thiosemicarbazide and 14.6 g (1.05 equiv) of ethoxymethylenemalononitrile in ethanol was allowed to stand overnight. The resultant solid, mp 135–137°, weighed 18.3 g (77.5%): ir 3.06 (NH), 4.51 μ (CN); nmr τ −0.23 (bt, 1, NH), 1.35 (bs, 2, NH_2), 2.10 (s, 1, CH=), 3.7–5.0 (m, 3, CH_2=CH–), 5.73 (bm, 2, CH_2=$CHCH_2$–).

Anal. Calcd for $C_8H_9N_5S$: C, 46.36; H, 4.38; N, 33.79. Found: C, 46.48; H, 4.31, N, 34.01.

Attempted Cyclization of 1a.—A solution of 5 g of **1a** in ethanol was held at reflux 10 days and then was cooled on ice. There was obtained 3.9 g of **1a**, mp 191–194°, the ir spectrum of which was identical with that of starting material.

Attempted Cyclization of 1b.—A solution of 5 g of **1b** in ethanol was held at reflux 110 hr. The odor of diethyl malonate was evident. The solid obtained, mp 241–243°, 0.5 g (24%), possessed an ir spectrum identical with that of authentic 1,6-diphenylbiurea (lit.[13] mp 242–243°).

2-Ethylamino-1,3,4-thiadiazole from 2a.—A solution of 15 g of **2a** in ethanol was held 28 hr at reflux. The solvent was removed under vacuum, and the residual oil was partially distilled to give 4.9 g (59%) of liquid distillate, bp 61–63° (2.5 mm), identified as diethyl malonate from the ir spectrum, and 5.0 g of pot residue. The residue was chromatographed on neutral, activity I alumina. With 2% ethanol in benzene 2.1 g (31%) of 2-ethylamino-1,3,4-thiadiazole, mp 70–71° (lit.[10] mp 70°), was eluted: ir 3.00 μ (NH), no C=O, strong 6.6-μ absorption; nmr τ 1.37 (s, 1, CH=), 2.28 (bs, 1, NH), 6.66 (m, 2, CH_2CH_3), 8.80 (t, 3, J = 7 Hz, CH_2CH_3).

(13) L. Horner and H. Fernekess, *Chem. Ber.*, **94**, 712 (1961).

2-Anilino-1,3,4-thiadiazole from 2c.—A solution of 5 g of **2c** in ethanol was held 24 hr at reflux. Concentration and cooling of the solution yielded 2-anilino-1,3,4-thiadiazole, 2.0 g (77%), mp 173–175° (lit.[10] mp 173°).

Ethyl 5-Amino-1-(methylcarbamoyl)-4-pyrazolecarboxylate (8a) from 3a.—A 15-g sample of **3a** in ethanol was held 18 hr at reflux and then was cooled on ice. The resultant solid, 5.6 g, mp 131–133°, was collected: ir 2.90, 2.99 (NH), 5.80 (C=O), 5.96 μ (ester C=O); nmr τ 1.98 (broad, 1 H, CH_3NH), 2.28 (s, 1, CH), 2.85 (broad, 2, NH_2), 5.77 (q, 2, J = 7 Hz, OCH_2CH_3), 7.19 (d, 3, J = 5 Hz, CH_3NH), 8.71 (t, 3, J = 7 Hz, OCH_2CH_3). The filtrate was held at reflux an additional 16 hr and was again cooled to produce another 2.6 g of solid, mp 131–133°. The total yield was 55%.

Anal. Calcd for $C_8H_{12}N_4O_3$: C, 45.28; H, 5.70; N, 26.40. Found: C, 45.58; H, 5.81; N, 26.14.

Ethyl 5-Amino-4-pyrazolecarboxylate from 3b.—A 15-g sample of **3b** in ethanol was held 16 hr at reflux and then was cooled on ice. The resultant solid, 0.3 g (4%), mp 245–247°, was identified from the ir spectrum as 1,6-diphenylbiurea. The filtrate was concentrated under vacuum, and the residue was crystallized from benzene to give 6.3 g (74%) of ethyl 5-amino-4-pyrazolecarboxylate, mp 100–102° (lit.[2] mp 102–103°), identified from the ir and nmr spectra: ir 2.90, 3.11 (NH), 6.00 μ (C=O); nmr τ −1.85 (b, 1, NH), 2.40 (s, 1, CH=), 4.22 (b, 2, NH_2), 5.82 (q, 2, J = 7 Hz, OCH_2CH_3), 8.76 (t, 3, J = 7 Hz, OCH_2CH_3).

Ethyl 5-Amino-1-(phenylcarbamoyl)-4-pyrazolecarboxylate (8b) from 3b.—A mixture of 12 g of **3b** and ethanol was held at reflux 6.5 hr, the resultant solution was cooled on ice, and 0.3 g of 1,6-diphenylbiurea, mp 238–241°, was collected. The filtrate was concentrated and cooled on ice to give 1.8 g (15%) of solid, mp 119–121°. This solid was crystallized from ethyl acetate to give 0.9 g of solid: mp 125–127°; ir 2.90, 3.02 (NH), 5.81 (C=O), 5.98 μ (ester C=O); nmr τ −0.20 (s, 1, NH), 2.05–2.95 (m, 8, C_6H_5, CH=, NH_2), 5.71 (q, 2, J = 7 Hz, OCH_2CH_3), 8.70 (t, 3, J = 7 Hz, OCH_2CH_3).

Anal. Calcd for $C_{13}H_{14}N_4O_3$: C, 56.93; H, 5.15; N, 20.43. Found: C, 56.74; H, 5.23; N, 20.29.

Ethyl 5-Amino-1-(ethylthiocarbamoyl)-4-pyrazolecarboxylate (9) from 4a.—A mixture of 10 g of **4a** and ethanol was held 1 hr at reflux. The solution was concentrated and cooled on ice to produce 5.9 g (59%) of **9**: mp 88–89°; ir 2.98, 3.07 (NH), 5.95 μ (C=O); nmr τ −0.12 (b, 1, NH), 1.82 (b, 2, NH_2), 2.21 (s, 1, CH=), 5.75 (q, 2, J = 7 Hz, OCH_2CH_3), 6.33 (q, 2, J = 7 Hz, NCH_2CH_3), 8.76 (m, 6, OCH_2CH_3, NCH_2CH_3).

Anal. Calcd for $C_{19}H_{14}N_4O_2S$: C, 44.61; H, 5.82; N, 23.12. Found: C, 44.78; H, 5.86; N, 23.16.

Cyclization of 4c.—A mixture of 5 g of **4c** in ethanol was held 11 hr at reflux and then was filtered hot to remove 0.4 g (14%) of 1,6-diphenyl-2,5-dithiobiurea (ir identification). The filtrate was concentrated under vacuum, and the residue was crystallized from benzene to give 0.6 g of unidentified solid. From the filtrate was obtained 0.5 g (19%) of impure 5-amino-4-pyrazolecarboxylate (ir identification).

Registry No.—**1a**, 19359-71-8; **1b**, 19359-72-9; **1c**, 19359-73-0; **2a**, 19359-74-1; **2b**, 19359-75-2; **2c**, 19359-76-3; **3a**, 19375-48-5; **3b**, 19375-49-6; **3c**, 19375-50-9; **4a**, 19375-51-0; **4b**, 19375-52-1; **4c**, 19375-53-2; **5a**, 19375-54-3; **5b**, 19375-55-4; **6a**, 19375-56-5; **6b**, 19375-57-6; **7a**, 19375-58-7; **7b**, 19375-59-8; **8a**, 19375-60-1; **8b**, 19375-61-2; **9**, 19375-62-3; 4-(3,4-dichlorophenyl)semicarbazide, 19375-63-4.