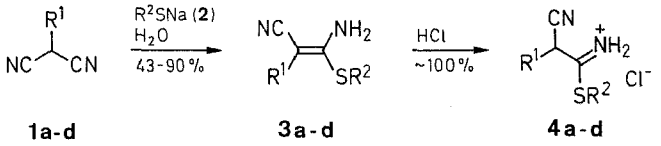
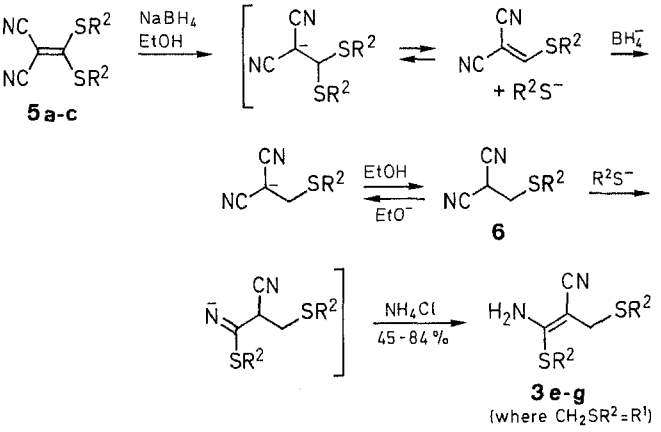
was reacted with a 15% aqueous solution of sodium methanethiolate (**2a**) to afford 3-amino-3-(methylthio)acrylonitrile **3a** in 90% yield. Compound **3a** was converted into its salt **4a** in quantitative yield on treatment with dry ethereal hydrogen chloride. When the present method was applied to the monosubstituted malononitriles **1b–d**, the corresponding compounds **3b–d** were formed in moderate yield.



1a-d **3a-d** **4a-d**

Next, we have developed a unique preparative method for **3**, which is described for **3e–g**. The method consists of the reduction of 3,3-bis(alkylthio)methylenemalononitriles **5** with sodium borohydride. The reaction is considered to proceed via



1–4	R^1	R^2	3	5, 6	R^2
a	H	CH_3	**e**	**a**	CH_3
b	CH_3	CH_3	**f**	**b**	CH_2Ph
c	*n*-Bu	CH_3	**g**	**c**	CH_2SiMe_3
d	CH_2Ph	CH_3			

the 1,3-transfer of an alkylthio group as follows. At first the hydride ion generated from sodium borohydride reacts with **5** in the Michael addition manner. After elimination of alkylthiolate anion, an additional attack of the hydride ion takes place followed by protonation to give the species **6**, which reacts with alkylthiolate anion resulting in the formation of **4**. In this reaction the presence of **6** was confirmed by TLC. By this method compounds **3e, 3f**, and **3g** were easily prepared from compounds **5a, 5b**, and **5c**, respectively (Table 1). A completely different procedure was used to prepare **2h**. Thus simple *S*-alkylation of phenyl(cyano)thioacetamide (**7**) with methyl iodide in the presence of sodium ethoxide in ethanol gave **2h** in good yield (Table 1).

Compounds **3** prepared by the above two methods were converted in quantitative yield into the corresponding salts **4** on treatment with dry hydrogen chloride in dry ether, which were used for the synthesis of heterocycles.

3,5-Diaminopyrazoles and 1,3,4-Oxadiazoles From Cyanoacetothioimidates

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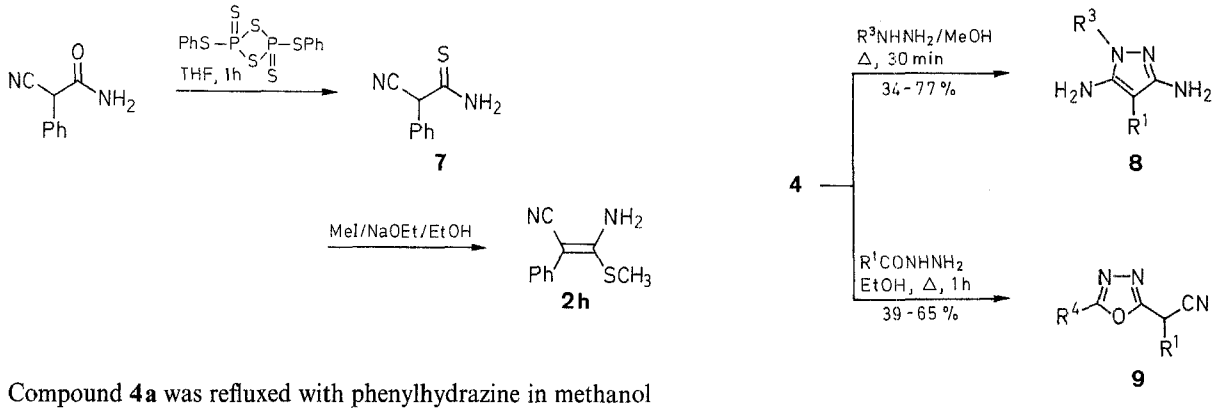
2-Substituted 3-amino-3-(methylthio)acrylonitriles cyanoketene *S,N*-acetals are synthesized by two convenient methods. The imino esters of their hydrochloride salts are found to be good starting materials for the synthesis of 4-substituted 3,5-diaminopyrazoles and 2,5-disubstituted 1,3,4-oxadiazoles.

The standard method for the synthesis of pyrazoles consists in the condensation of 1,3-difunctional compounds with hydrazine or its derivatives.[1] In many 1,3-difunctional compounds used for this purpose, the imino esters have been reported to be useful for the synthesis of 3,5-diaminopyrazoles.[2] Our knowledge on the good leaving ability of alkylthio group[3] led us to synthesize and employ the thioimino esters instead of the imino esters.

Then we intended to obtain the cyanoacetothioimidate hydrochloride from the reaction of malononitrile with *n*-butylmercaptan in the presence of hydrochloric acid. However this reaction proceeded in low yield (42%) and this method further required the use of expensive and bad-smelling mercaptans.

To avoid these drawbacks we developed the following recommended method: An alcoholic solution of malononitrile **1a**



Compound **4a** was refluxed with phenylhydrazine in methanol to give a hydrochloride salt of *N*-phenyl-3,5-diaminopyrazole **8a** in 77% yield. This yield is about 3.5 times as much as that of literature,[2] in which methyl cyanoacetimidate hydrochloride has been employed. Two 3,5-diaminopyrazoles were synthesized by this method (Table 2). We also found that **4a** reacted with benzoic acid hydrazide in refluxing ethanol to form 2-cyanomethyl-5-phenyl-1,3,4-oxadiazole **(9a)** in 65% yield (Table 3).

Unfortunately, the hydrochloride salts of **3e, 3f**, and **3g** did not give fruitful results in these reactions. This is perhaps because they exist mainly in enol forms.

In conclusion, compounds **4** are proved to be good starting materials for the syntheses of 4-substituted 3,4-diaminopyrazoles and 2,5-disubstituted 1,3,4-oxadiazoles.[4]

Table 1. 2-Substituted 3-Amino-3-(methylthio)acrylonitriles **3** Prepared

Product[a]	Yield[b] (%)	mp[c] (°C)	Molecular Formula[d]	MS (M^+)[e] *m/z*	IR (neat)[f] ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[g] δ, *J* (Hz)
3a	90	oil	$C_4H_6N_2S$ (114.2)	114	3450, 3320, 3200, 2200	2.36, 2.45 (s, 3H); 3.85, 4.26 (s, 1H); 4.80, 5.40 (br, 2H)
3b	43	oil	$C_5H_8N_2S$ (128.2)	128	3450, 3330, 3220, 2190	1.54 (s, 3H); 2.16, 2.20 (s, 3H); 4.55 (br, 2H
3c	53	oil	$C_8H_{14}N_2S$ (170.3)	170	3400, 3320, 3160, 2910, 2850, 2180	0.90 (m, 3H); 1.20–1.60 (m, 4H); 1.80–2.20 (m, 2H); 2.16–2.20 (s, 3H); 4.54 (br, 2H
3d	63	oil	$C_{11}H_{12}N_2S$ (204.3)	204	3420, 3310, 3200, 3000, 2900, 2175	2.11, 2.12 (s, 3H); 3.32, 3.42 (s, 2H); 4.70 (br, 2H); 7.08 (s, 5H)
3e	84	oil	$C_6H_{10}N_2S_2$ (174.3)	127[h]	3400, 3300, 3190, 2900, 2160	1.65, 2.04 (s, 3H); 2.28, 2.35 (s, 3H); 3.16, 3.20 (s, 2H); 4.20, 4.80 (br, 2H)
3f	48	oil	$C_{18}H_{18}N_2S_2$ (326.5)	203[i]	3420, 3310, 3200, 3020, 2960, 2190	2.92, 3.04 (s, 2H); 3.36, 3.44 (s, 2H); 3.75, 3.80 (s, 2H); 4.60 (br, 2H); 6.80 (s, 10H)
3g	45	106–107	$C_{12}H_{26}N_2S_2Si_2$ (318.6)	199[j]	3380, 3270, 3160, 2930, 2160	0.08, 0.15 (s, 18H); 1.75, 1.77 (s, 2H); 2.04, 2.12 (s, 2H); 3.26, 3.30 (s, 2H); 4.88, 5.10 (br, 2H)
3h	87	111–112	$C_{10}H_{10}N_2S$ (190.3)	190	3440, 3300, 3190, 3040, 2175	2.24 (n, 3H); 4.70 (br, 2H); 7.28 (m, 5H)

[a] A mixture of *E*- and *Z*-isomers.
[b] Yield of isolated product.
[c] Corrected.
[d] Satisfactory microanalyses obtained: C ±0.30, H ±0.30, N ±0.30.
[e] Recorded on a Hitachi M-60 spectrometer.
[f] Recorded on a Hitachi 215 spectrometer.
[g] Recorded on a JOEL MH-100 instruments.
[h] $M^+ - SCH_3$.
[i] $M^+ - SCH_2Ph$.
[j] $M^+ - SCH_2SiMe_3$.

Table 2. 3,5-Diaminopyrazoles **8** Prepared

Product	R^1	R^3	Yield[a] (%)	mp[b] (°C)	Molecular Formula[c]	MS (M^+)[d] *m/z*	IR (KBr)[e] ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[f] δ, *J* (Hz)
8c	$PhCH_2$	Ph	35	133–134	$C_{16}H_{16}N_4$ (264.3)	264	3400, 3320, 3250, 3120, 1620	3.48 (br, 4H); 3.62 (s, 2H); 7.25 (m, 7H); 7.5 (m, 3H)
8d	*n*-Bu	Ph	34	62–62	$C_{13}H_{18}N_4$ (230.3)	230	3410, 3300, 3180, 2940, 2910, 2840, 1620	0.96 (t, 3H, *J* = 6); 1.48 (m, 4H); 2.24 (t, 2H, *J* = 6); 3.54 (br, 4H); 7.26 (m, 2H); 7.44 (m, 3H)

[a–f] Corresponds to b–g in Table 1.

Table 3. 1,3,4-Oxadiazoles **9** Prepared

Product	R^1	R^4	Yield[a] (%)	mp[b] (°C)	Molecular Formula[c]	MS (M^+)[d] *m/z*	IR (KBr)[e] ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[f] δ, *J* (Hz)
9a	H	Ph	65	121	$C_{10}H_7N_3O$ (185.2)	185	2925, 2255	3.95 (s, 2H); 7.20 (m, 3H); 7.66 (m, 2H)
9b	H	*n*-$C_{11}H_{23}$	39	87–88	$C_{15}H_{25}N_3O$ (263.4)	263	2950, 2920, 2850, 2270	0.86 (m, 3H); 1.25 (br s, 16H); 1.90 (m, 2H); 2.84 (t, 2H, *J* = 7); 4.00 (s, 2H)
9c	*n*-Bu	Ph	59	*oil*	$C_{14}H_{15}N_3O$ (241.3)	241	3050, 2950, 2850, 2250	0.92 (m, 2H); 1.50 (m, 4H); 2.15 (m, 2H); 4.20 (t, 1H, *J* = 7); 7.35 (m, 3H); 7.8 (m, 2H)
9d	$PhCH_2$	Ph	41	86–87	$C_{17}H_{13}N_3O$ (275.3)	224	3050, 3020, 2250	3.35 (d, 2H, *J* = 7); 4.36 (t, 1H, *J* = 8); 7.05 (s, 5H); 7.3 (m, 3H); 7.7 (m, 2H)
9e	H	2-indolyl	50	224–227 (dec)	$C_{12}H_8N_4O$ (224.2)	224	3180, 2930, 2900, 2260	4.4 (s, 2H); 7.02 (m, 3H); 7.44 (m, 2H); 12.06 (br, 1H)

[a–f] Corresponds to b–g in Table 1.

2-Methylmalononitrile (1b):
A mixture of P_2O_5 (5 g, 17.5 mmol), hexamethyldisiloxane (13 mL, 65 mmol), and dry benzene (25 mL) is heated at reflux for 0.5 h under argon. To this polyphosphate solution[5] is added 2-(methyl)cyanoacetamide[6] (800 mg, 10 mmol). The mixture is refluxed for 1 h and then cooled to room temperature. The mixture is added to sat. $NaHCO_3$ solution (20 mL) and then extracted with benzene (2 × 10 mL). The extract is washed with brine, dried ($MgSO_4$), and evaporated. The residue is purified by bulb to bulb distillation to give **1b** as a colorless oil; yield: 624 mg (78%); bp 88–89 °C/27 mbar (bath temp); (Lit.[6] bp 197–198 °C/1 bar).

2-*n*-Butylmalononitrile (1c):
Prepared from 2-(*n*-butyl)cyanoacetamide[7] (1.4 g, 10 mmol) and polyphosphate solution as described above; yield: 1.0 g (82%); bp 118–120 °C/26 mbar (Lit.[8] bp 120 °C/26 mbar).

2-Benzylmalononitrile (1d):
Prepared from 2-(benzyl)malonamide[9] (1.92 g, 10 mmol) and polyphosphate solution as described above; yield: 1.39 g (89%); bp 88–90 °C/0.4 mbar (Lit.[10] bp 174 °C/30 mbar).

3,3-Bis(methylthio)methylenemalononitrile (5a):
Compound **5a** is prepared from bis(sodiomercapto)methylenemalononitrile hydrate[11] and methyl iodide according to the reported procedure.[11] Similarly, **5b** and **5c** are obtained by the reaction of bis(sodiomercapto)methylenemalononitrile hydrate with benzyl chloride and (iodomethyl)trimethylsilane [or (chloromethyl)trimethylsilane and sodium iodide], respectively.

5a: mp 87–88 °C.

$C_{18}H_{17}N_2S_2$	calc.	C 66.44	H 5.27	N 8.60	S 19.70	
(325.4)	found	66.41	5.32	8.77	19.81	

5b: mp 67–68 °C

$C_{12}H_{22}N_2Si_2S_2$	calc.	C 45.81	H 7.05	N 8.90	Si 17.85	S 20.38
(314.6)	found	45.66	7.12	8.80	17.93	20.50

2-Substituted 3-Amino-3-(methylthio)acrylonitriles 3a–d; General Procedure:
To a mixture of the appropriate 2-substituted malononitrile **1a–d** (5 mmol) and absolute EtOH (5 mL) is added a commercial 15% aq. CH_3SNa solution[12] (5 mL) at 0 °C. The mixture is warmed to 10 °C and stirred for 30 min. The mixture is quenched with sat. NH_4Cl solution (10 mL) and then extracted with ether (3 × 15 mL). The combined extract is washed with brine, dried ($MgSO_4$), and evaporated. The residue is purified by TLC on silica gel (EtOAc/hexane as eluent).

2-Substituted 3-Amino-3-(methylthio)acrylonitriles 3e–g; General Procedure:
To a mixture of the appropriate 3,3-bis(alkylthio)methylenemalononitrile **5a–c** (5 mmol) and absolute EtOH (15 mL) is added $NaBH_4$ (186 mg, 5 mmol); the mixture is stirred for 30 min at 0 °C, and worked up as above.

Phenyl(cyano)thioacetamide (7):
A mixture of phenyl(cyano)acetamide[13] (320 mg, 2 mmol) and 2,4-bis(phenylthio)-1,3-dithia-2,4-diphosphetane 2,4-disulfide[14] (450 mg, 1.1 mmol) is stirred in THF (5 mL) for 1 h at room temperature. The mixture is evaporated to give a yellow oil, which is chromatographed in silica gel (EtOAc/hexane 1:1 as eluent); yield: 258 mg (73%); mp 151–154 °C (benzene).

3-Amino-2-phenyl-3-(methylthio)acrylonitrile (2h):
A mixture of **7** (176 mg, 1 mmol) and NaOEt (102 mg, 1.5 mmol) is stirred in absolute EtOH (5 mL) for 30 min at room temperature. The mixture is cooled and treated with MeI (0.5 mL, 3.2 mmol). The mixture is stirred for 12 h at room temperature and then evaporated. The residue is treated with sat. NH_4Cl solution and extracted with EtOAc (3 × 10 mL). The extract is washed with brine, dried ($MgSO_4$), and evaporated; yield: 165 mg (87%); mp 111–112 °C (benzene).

2-Substituted Cyanoacetothioimidate Hydrochloride Salts 4a–h; General Procedure:
Dry HCl gas is bubbled through a solution of 3-amino-3-(methylthio)acrylonitriles **2a–h** (5 mmol) in dry ether (15 mL) for 15 min. The mixture is stirred for 2 h at room temperature to give the corresponding hydrochlorides quantitatively.

1-Phenyl-3,5-diaminopyrazole Hydrochloride Salt (8a):
To a mixture of **4a** (150 mg, 1 mmol) and MeOH (5 mL) is added phenylhydrazine (0.1 mL, 1 mmol). The mixture is refluxed for 30 min, the solvent is evaporated, and the residue is recrystallized from EtOH/ether to give **8a** as white powder; yield: 162 mg (77%); mp 232–233 °C (dec) (Lit.[2] mp 229–230 °C, dec).

1-Phenyl-3,5-diaminopyrazoles 8c, d; General Procedure:
To a mixture of **3c, d** (1 mmol) and MeOH (5 mL) is added phenylhydrazine (0.1 mL, 1 mol). The mixture is refluxed for 30 min and then evaporated. The residue is treated with a mixture of EtOH/ether and then filtered. The filtrate is evaporated to give a syrup, which is purified by preparative TLC on silica gel (EtOAc).

1,3,4-Oxadiazoles 9a–e; General Procedure:
A mixture of **3a, c, d** (1 mmol) and carboxylic acid hydrazide (1 mmol) is stirred for 1 h in refluxing EtOH. The mixture is poured into water and extracted with EtOAc (3 × 15 mL). The combined extract is washed with brine, dried ($MgSO_4$), and evaporated. The residue is purified by preparative TLC on silica gel (EtOAc/hexane) (Table 3).

We thank Professor Y. Murakami (Toho University) for a generous gift of indoles.

Received: 8 March 1988; revised: 16 May 1988

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