

Jamin Huang* and Michael D. Graves [#]

Rhône-Poulenc Ag Company, P. O. Box 12014, T. W. Alexander Drive,
Research Triangle Park, North Carolina 27709

Received April 13, 1987

The formation of thiazolidinethiones **3** and/or imidazolidinedithiones **5** from cyanothioformanilides and aryl isothiocyanates is found to be dependent upon the type of bases used, reaction temperature and the nature and position of substituents on cyanothioformanilides. Examples are presented.

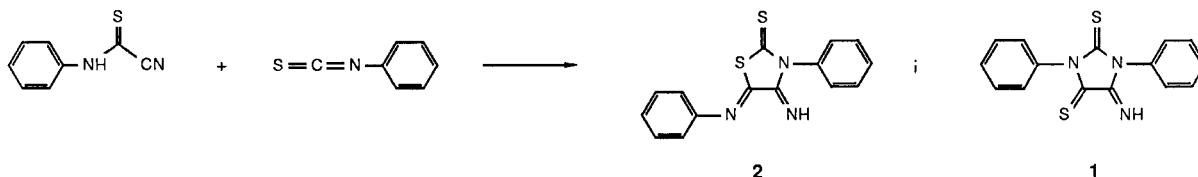
J. Heterocyclic Chem., **24**, 1781 (1987).

Recent interest [1,2] in thiazolidinethiones and imidazolidinedithiones prompts us to report the results of our investigation. The structure previously assigned to the product resulting from the reaction of *N*-phenylcyanothioformanilide and phenyl isothiocyanate in the presence of triethylamine at 5° was recently revised by Khattak *et al* [1] from imidazolidinedithione **1** [2] to thiazolidinethione **2** (Scheme I). Our work in this area has independently led us to the same conclusion. Here, we present additional ex-

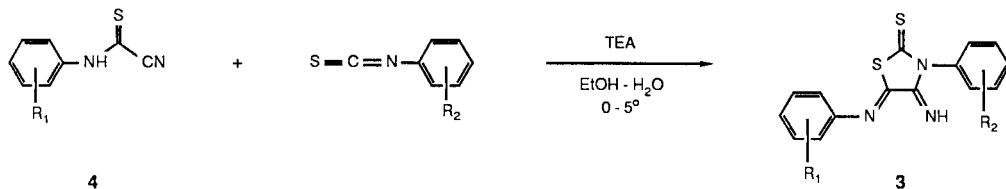
amples and confirmatory ¹³C nmr and mass spectral data supporting the structural assignment to the products obtained from this general reaction, and furthermore to report the subtle substituent and temperature effects which can alter the course of the reaction to produce either imidazolidinedithiones or thiazolidinethiones.

Thiazolidinethiones **3a-3l** were prepared by a procedure similar to that reported by Ketcham and Schaumann [2] (Scheme II). The ¹³C nmr chemical shifts

Scheme 1



Scheme II



	R ₁	R ₂
3a	3 - Cl	3 - Cl
3b	H	3 - Cl
3c	H	3,4 - Cl
3d (2)	H	H
3e	3,4 - Cl	H
3f	2 - <i>i</i> -C ₃ H ₇	3 - Cl
3g	2 - CH ₃	3 - Cl
3h	H	2 - CH ₃ , 4 - Cl
3i	H	3 - CH ₃
3j₁	2 - OCH ₃ , 5 - Cl	3 - Cl
3j₂	2 - OCH ₃ , 5 - Cl	4 - OCH ₃
3k	4 - OCH ₃	3 - Cl
3l	4 - N(CH ₃) ₂	3 - Cl

of the three carbons on the heterocyclic ring of these molecules are consistent with the assigned structure [1]. Moreover, mass spectral analysis of **3a** showed a loss of carbon disulfide moiety from the molecular ion, which is only consistent with the thiazolidinethione structure [3]. High resolution mass spectrum peak match of *m/e* 365 (molecular ion) and *m/e* 288 (molecular ion - carbon disulfide -proton) has supported their compositions [4].

Although triethylamine has efficiently catalyzed most of the reactions in Scheme II, in the case of *N*-(4-dimethylaminophenyl)cyanothioformanilide (**4l**), a stronger base such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was necessary to effect the formation of thiazolidinethione (**3l**). This was not the case with the methoxy substituent in **4j** and **4k**.

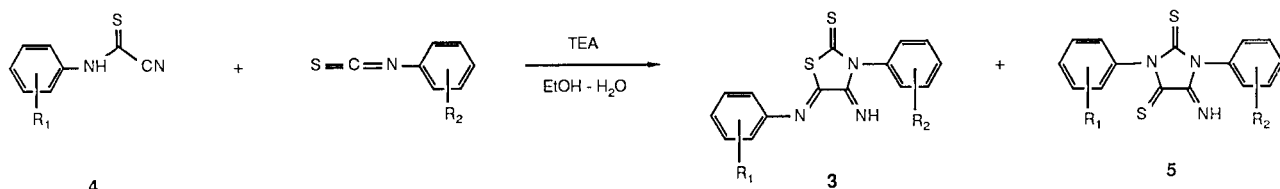
Furthermore, we have also found that the course of the reaction leading to either thiazolidinethiones **3**, or imidazolidinedithiones **5**, or a mixture of both, is strongly influenced by reaction temperature and the nature and position of substituents on the cyanothioformanilides **4**. The temperature effect on the reaction course was studied with selected compounds. The specific reactions, temperature and product distribution are shown in Table I. In general, higher reaction temperature tends to promote the formation of imidazolidinedithiones **5** as shown in reaction no. 1 vs. 2, 3 vs. 4, or 11 vs. 12. The amount of imidazolidinedithiones formed is highly dependent upon the nature and

position of substituents on the cyanothioformanilide **4**. For example, in the reaction with 3-chlorophenyl isothiocyanate, **4f** produced only thiazolidinethione **3f** (reaction No. 9, 10) and **4m** produced solely imidazolidinedithione **5m** (reaction No. 13, 14) at either 0° or room temperature. When reacted with **4j**, thiazolidinethione **3jl** was formed at 0° (reaction No. 3) whereas its isomeric imidazolidinedithione **5jl** was formed at room temperature (reaction No. 4).

Substituents on the phenyl isothiocyanate appear to have some effect on reaction rate, but have a minimal effect on reaction course. This is demonstrated by the similar product distribution observed from the reactions No. 3-6 and possibly No. 8 in Table I. No products were found in reaction No. 7. Substituents at the *ortho* position of phenyl isothiocyanate appear to slow the reaction rate. This was also observed on the formation of thiazolidinethione **3h** in Scheme II. Unlike most of the reactions in Scheme II, the reaction of *N*-phenylcyanothioformanilide and 2-methyl-4-chlorophenyl isothiocyanate proceeded very slowly at 0° and efficient formation of **3h** was only achieved at room temperature.

In order to determine whether the formation of different products with different conditions as shown in Table I is a reflection of kinetic vs. thermodynamic control, experiments were conducted by stirring a solution of thiazolidinethione **3jl** and 95% ethanol with a catalytic

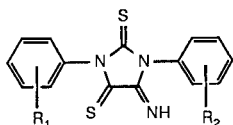
Table I

Effect of R₁ Substituent and Temperature on the Reaction of Cyanothioformanilides **4** and Phenyl isothiocyanates

Reaction No.	R ₁	R ₂	Reaction Temperature	Product Distribution	
				3	5
1	H (4c)	3,4-Cl	-5°	3c	—
2	"	"	40°	3c (major)	5c (minor)
3	2-OCH ₃ , 5-Cl (4j)	3-Cl	0°	3jl	—
4	"	"	RT	—	5jl
5	"	4-OCH ₃	0°	3j2	—
6	"	"	RT	—	5j2
7	"	2-CH ₃ , 4-Cl	0°	no reaction	
8	"	"	RT	—	5j3
9	2- <i>i</i> -C ₃ H ₇ (4f)	3-Cl	0°	3f	—
10	"	"	RT	3f	—
11	4-OCH ₃ (4k)	3-Cl	0°	3k	—
12	"	"	RT	3k (major)	5k (minor)
13	2-OCH ₃ (4m)	3-Cl	0°	—	5m
14	"	"	RT	—	5m
15	2,4-OCH ₃ (4n)	3-Cl	RT	—	5n
16	2,4,6-CH ₃ (4o)	3-Cl	RT	—	5o

amount of triethylamine at room temperature for 18 hours. After removal of solvents, ^{13}C nmr spectrum of the crude residue indicated the disappearance of thiazolidinethione **3j1** and the formation of its isomeric imidazolidinedithione **5j1**. This isomerized **5j1** was further purified by chromatography and its identity was confirmed. Isomerization of **3j1** to **5j1** did not occur in the absence of triethylamine.

Although some imidazolidinedithiones could be prepared selectively by adjusting the reaction temperature as shown in Table I, this general application to the synthesis of these materials is still somewhat limited because of the strong dependence on the nature and the position of the substituents on cyanothioformanilides **4**. However, imidazolidinedithiones can be prepared exclusively by using catalytic amounts of sodium hydride in tetrahydrofuran at 0° . The previous investigators also reported the formation of imidazolidinedithione **1** by employing sodium hydride and a crown ether [1]. The identity of the products reported herein was unambiguously determined based on ^{13}C nmr chemical shift patterns of the three carbons of the heterocyclic moiety of imidazolidinedithiones **5** [5].



5

	R ₁	R ₂
5c	H	3,4-Cl
5j1	2-OCH ₃ , 5-Cl	3-Cl
5j2	2-OCH ₃ , 5-Cl	4-OCH ₃
5j3	2-OCH ₃ , 5-Cl	2-CH ₃ , 4-Cl
5l	4-N(CH ₃) ₂	3-Cl
5m	2-OCH ₃	3-Cl
5n	2,4-OCH ₃	3-Cl
5o	2,4,6-CH ₃	3-Cl
5p	4-Cl	3-Cl

Conclusion.

During the synthesis of a limited series of the heterocyclic compounds reported herein for biological evaluations, it was noted that the formation of thiazolidinethiones **3** and/or imidazolidinedithiones **5** from arylcyanothioformanilides **4** and aryl isothiocyanates is strongly dependent upon the type of bases used, reaction temperature and the nature and position of substituents on cyanothioformanilides. The biological properties of these molecules will be presented in a separate report.

EXPERIMENTAL

N-Arylcyanothioformanilides **4** were prepared according to the procedure reported by Kumelj and Tišler [6]. The melting points are uncorrected. The ^{13}C nmr spectra were recorded at 22.5 MHz with a JEOL FX

90Q fourier transform spectrometer. Microanalyses were performed by Galbraith Laboratories, Inc. Infrared spectra were recorded on a Perkin-Elmer 197 spectrometer. The ^{13}C nmr chemical shift patterns of the three carbons of the heterocyclic moiety of thiazolidinethiones **3** and imidazolidinedithiones **5** are easily distinguishable and are highly characteristic of either structure. Reaction yields reported here have not been optimized.

3-(3,4-Dichlorophenyl)-4-imino-5-(phenylimino)-2-thiazolidinethione (**3c**).

This compound was prepared by a procedure similar to that reported by Ketcham and Schaumann [2]. Triethylamine (15.1 ml) was added to a solution of *N*-phenylcyanothioformanilide **4c** (75.0 g), 3,4-dichlorophenyl isothiocyanate (34.4 g) and 95% ethanol (615 ml) at 0° . This reaction solution was stirred at 0° for 5 minutes. A yellow solid began to precipitate after 15 minutes standing. After an additional two hours standing at 0° , 46 ml of water was added and the resulting suspension mixture was allowed to stand at 0° for a period of 45 minutes. The mixture was filtered and the solid was washed with a small amount of 95% ethanol. Thiazolidinethione **3c** (146.5 g, 87%) as a yellow solid was obtained, mp $146-150^\circ$; ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 192.5, 159.0, 150.6, 148.2, 135.8, 132.1, 131.4, 131.2, 131.1, 129.9, 129.6, 127.3 and 120.1 ppm; ir (dichloromethane): 3280, 1650, 1633, 1590 cm^{-1} .

Anal. Calcd. for $\text{C}_{15}\text{H}_9\text{Cl}_2\text{N}_3\text{S}_2$: C, 49.19, H, 2.48; N, 11.47. Found: C, 49.15; H, 2.43; N, 11.40.

3-(3-Chlorophenyl)-4-imino-5-(3-chlorophenylimino)-2-thiazolidinethione (**3a**).

This compound was prepared from *N*-(3-chlorophenyl)cyanothioformanilide (**4a**) and 3-chlorophenyl isothiocyanate according to Scheme II, mp $140-143^\circ$. ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 190.8 (s), 158.8 (s), 152.8 (s), 149.9 (s), 137.2 (s), 134.1 (s), 133.2 (s), 131.6 (d), 130.8 (d), 129.3 (d), 128.8 (d), 127.8 (d), 126.8 (d), 119.9 (d) and 118.3 (d) ppm; ir (dichloromethane): 3275, 1643, 1630, 1580 cm^{-1} .

Anal. Calcd. for $\text{C}_{15}\text{H}_9\text{Cl}_2\text{N}_3\text{S}_2$: C, 49.19; H, 2.48; N, 11.47. Found: C, 49.28; H, 2.49; N, 11.59.

3-(3-Chlorophenyl)-4-imino-5-(phenylimino)-2-thiazolidinethione (**3b**).

This compound was prepared from *N*-phenylcyanothioformanilide and 3-chlorophenyl isothiocyanate according to Scheme II, mp $105-108^\circ$; ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 192.5, 159.3, 150.8, 148.3, 137.4, 133.2, 130.8, 129.9, 129.3, 128.9, 127.9, 127.3 and 120.1 ppm; ir (dichloromethane): 3280, 1650, 1630, 1590 cm^{-1} .

Anal. Calcd. for $\text{C}_{15}\text{H}_9\text{ClN}_3\text{S}_2$: C, 54.29; H, 3.04; N, 12.66. Found: C, 54.01; H, 2.97; N, 12.43.

3-Phenyl-4-imino-5-(3,4-dichlorophenylimino)-2-thiazolidinethione (**3e**).

This compound was prepared from *N*-(3,4-dichlorophenyl)cyanothioformanilide and phenyl isothiocyanate according to Scheme II, mp $136-139^\circ$; ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 191.5, 159.1, 153.7, 148.4, 135.9, 132.2, 131.8, 129.3, 129.2, 128.6, 122.0 and 120.1 ppm; ir (dichloromethane): 3280, 1650, 1630, 1585 cm^{-1} .

Anal. Calcd. for $\text{C}_{15}\text{H}_9\text{Cl}_2\text{N}_3\text{S}_2$: C, 49.19; H, 2.48; N, 11.47. Found: C, 49.09; H, 2.54; N, 11.42.

3-(3-Chlorophenyl)-4-imino-5-(2-isopropylphenylimino)-2-thiazolidinethione (**3f**).

This compound was prepared from *N*-(2-isopropylphenyl)cyanothioformanilide and 3-chlorophenyl isothiocyanate similar to that of **3c**, mp $140-143^\circ$; ^{13}C nmr (deuteriochloroform): δ 192.1, 160.5, 149.8, 146.0, 142.1, 136.5, 135.2, 136.0, 130.0, 129.0, 128.0, 126.9, 126.8, 126.6, 116.7, 28.6 and 23.2 ppm; ir (dichloromethane): 3280, 1648, 1630, 1590 cm^{-1} .

Anal. Calcd. for $\text{C}_{18}\text{H}_{16}\text{ClN}_3\text{S}_2$: C, 57.82; H, 4.31; N, 11.24. Found: C, 57.59; H, 4.32; N, 11.16.

3-(3-Chlorophenyl)-4-imino-5-(2-methylphenylimino)-2-thiazolidinethione (**3g**).

This compound was prepared from *N*-(2-methylphenyl)cyanothioformanilide and 3-chlorophenyl isothiocyanate according to Scheme II,

mp 115-117°; ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 192.7, 159.1, 150.6, 147.4, 137.4, 133.2, 131.1, 130.8, 130.4, 129.3, 129.0, 127.9, 127.1, 116.8 and 17.3 ppm; ir (dichloromethane): 3380, 1630 (br), 1590 cm^{-1} .

Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{ClN}_3\text{S}_2$: C, 55.56; H, 3.50; N, 12.15. Found: C, 55.38; H, 3.45; N, 12.21.

3-(2-Methyl-4-chlorophenyl)-4-imino-5-(phenylimino)-2-thiazolidinethione (**3h**).

This compound was prepared from *N*-phenylcyanothioformanilide and 2-methyl-4-chlorophenyl isothiocyanate similar to Scheme II, except for reaction temperature (at ambient temperature), mp 170-171°; ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 191.8, 158.4, 150.5, 148.3, 138.6, 134.1, 134.0, 130.7, 130.5, 129.8, 127.3, 127.1, 120.2 and 16.9 ppm; ir (dichloromethane): 3280, 1650, 1630, 1570 cm^{-1} .

Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{ClN}_3\text{S}_2$: C, 55.56; H, 3.50; N, 12.15. Found: C, 55.54; H, 3.42; N, 12.30.

3-(3-Methylphenyl)-4-imino-5-(phenylimino)-2-thiazolidinethione (**3i**).

This compound was prepared from *N*-phenylcyanothioformanilide and 3-methylphenyl isothiocyanate according to Scheme II, mp 135-138°; ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 192.3, 159.4, 151.0, 148.4, 138.7, 135.9, 129.8, 129.0, 128.9, 127.2, 125.7, 120.1 and 20.7 ppm; ir (dichloromethane): 3280, 1650, 1635, 1592 cm^{-1} .

Anal. Calcd. for $\text{C}_{16}\text{H}_{13}\text{N}_3\text{S}_2$: C, 61.71; H, 4.21; N, 13.49. Found: C, 61.68; H, 4.33; N, 13.45.

3-(3-Chlorophenyl)-4-imino-5-(2-methoxy-5-chlorophenyl)-2-thiazolidinethione (**3j1**).

This compound was synthesized similar to that of **3c**. A reaction mixture of *N*-(2-methoxy-5-chlorophenyl)cyanothioformanilide **4j** (6.06 g), 3-chlorophenyl isothiocyanate (4.53 g), triethylamine (0.87 ml) and 95% ethanol (500 ml) was stirred at 0° for 3 hours and stored in the refrigerator overnight. The resulting suspension mixture was filtered and thiazolidinethione **3j1** (3.0 g, 28%) was obtained, mp 150-153°; ^{13}C nmr (deuteriochloroform): δ 191.3, 160.3, 152.4, 148.5, 137.7, 136.5, 135.2, 130.5, 130.0, 129.0, 127.9, 126.9, 126.0, 120.8, 113.1 and 55.9 ppm; ir (dichloromethane): 3280, 1630 (br), 1590 cm^{-1} ; high resolution ms at *m/e* 395 (M^+): 394.9730. (Calcd for $\text{C}_{16}\text{H}_{11}\text{Cl}_2\text{N}_3\text{O}_2\text{S}_2$: 394.9722).

Anal. Calcd. for $\text{C}_{16}\text{H}_{11}\text{Cl}_2\text{N}_3\text{O}_2\text{S}_2$: C, 48.49; H, 2.80; N, 10.60. Found: C, 47.66; H, 2.82; N, 10.39. Several attempts to obtain correct carbon analysis for the chromatography purified sample of **3j1** proved to be unsatisfactory, possibly due to instability.

3-(4-Methoxyphenyl)-4-imino-5-(2-methoxy-5-chlorophenyl)-2-thiazolidinethione (**3j2**).

This compound was prepared from *N*-(2-methoxy-5-chlorophenyl)cyanothioformanilide and 4-methoxyphenyl isothiocyanate similar to that of **3j1**, mp 103-104°, 20% yield; ^{13}C nmr (deuteriochloroform): δ 191.9, 160.8, 160.2, 153.1, 148.6, 138.0, 129.5, 128.0, 127.8, 126.0, 120.7, 115.0, 113.1, 56.0 and 55.5 ppm; ir (dichloromethane): 3270, 1630 (br), 1585 cm^{-1} .

Anal. Calcd. for $\text{C}_{17}\text{H}_{14}\text{ClN}_3\text{O}_2\text{S}_2$: C, 52.10; H, 3.60; N, 10.72. Found: C, 52.11; H, 3.63; N, 10.61.

3-(3-Chlorophenyl)-4-imino-5-(4-methoxyphenylimino)-2-thiazolidinethione (**3k**).

This compound was prepared from *N*-(4-methoxyphenyl)cyanothioformanilide and 3-chlorophenyl isothiocyanate according to Scheme II, mp 127-128°; ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 192.7, 159.8, 158.8, 146.9, 140.2, 137.4, 133.2, 130.8, 129.2, 128.9, 127.9, 123.1, 115.0 and 55.4 ppm; ir (dichloromethane): 3270, 1645, 1620, 1590 cm^{-1} .

Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{ClN}_3\text{O}_2\text{S}_2$: C, 53.11, H, 3.34; N, 11.61. Found: C, 53.16; H, 3.62; N, 11.59.

3-(3-Chlorophenyl)-4-imino-5-(4-dimethylaminophenylimino)-2-thiazolidinethione (**3l**).

1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 4.08 g) was added to the solution of *N*-(4-dimethylaminophenyl)cyanothioformanilide **4l** (11.0 g),

3-chlorophenyl isothiocyanate (9.1 g) and 95% ethanol (200 ml) at 0°. The reaction mixture was stirred at 0° for 2 hours and stored in a refrigerator overnight. The resulting suspension mixture was filtered and thiazolidinethione **3l** (6.0 g, 30%) was obtained, mp 135-139°; ^{13}C nmr (deuteriochloroform): δ 192.8, 161.8, 150.4, 139.3, 136.9, 135.1, 134.0, 138.2, 129.7, 129.0, 127.0, 125.4, 112.1 and 40.2 ppm.

Anal. Calcd. for $\text{C}_{17}\text{H}_{15}\text{ClN}_4\text{S}_2$: C, 54.46; H, 4.03; N, 14.94. Found: C, 53.99; H, 4.24; N, 14.78.

1-(3-Chlorophenyl)-3-(4-dimethylaminophenyl)-5-imino-2,4-imidazolidinedithione (**5l**).

This compound was synthesized according to a similar procedure reported by Khattak *et al* [1]. Sodium hydride (1.07 g, 60% in oil dispersion) was added portionwise to the solution of *N*-(4-dimethylaminophenyl)cyanothioformanilide **4l** (11.0 g), 3-chlorophenyl isothiocyanate (9.1 g) and tetrahydrofuran (200 ml) at 0°. This reaction mixture was stirred at 0° for 2 hours and was stored in a refrigerator overnight. Tetrahydrofuran was removed *in vacuo* and the residue was partitioned between dichloromethane and saturated ammonium chloride aqueous solution. The dichloromethane layer was dried over magnesium sulfate, filtered and concentrated *in vacuo*. The crude residue was chromatographed on Florisil (100-200 mesh) utilizing a hexane-ethyl acetate gradient elution to afford imidazolidinedithione **5l** (6.13 g, 30%) as a black solid, mp 146-149°. This reaction yield was improved by employing lesser amounts, such as 0.1-0.05 equivalents, of sodium hydride; ^{13}C nmr (deuteriochloroform): δ 180.7, 180.1, 156.3, 150.8, 135.2, 134.8, 130.3, 129.6, 128.8, 128.5, 126.7, 123.0, 111.8 and 48.2 ppm; ir (dichloromethane): 3250, 1660, 1610, 1590 cm^{-1} .

Anal. Calcd. for $\text{C}_{17}\text{H}_{15}\text{ClN}_4\text{S}_2$: C, 54.46; H, 4.03; N, 14.94. Found: C, 54.53, H, 4.19; N, 14.89.

1-(3,4-Dichlorophenyl)-3-phenyl-5-imino-2,4-imidazolidinedithione (**5c**).

This compound was prepared from *N*-phenylcyanothioformanilide and 3,4-dichlorophenyl isothiocyanate similar to that of **5l**, mp 141-143°; ^{13}C nmr (deuteriochloroform): δ 179.7, 179.6, 155.9, 135.0, 133.9, 133.3, 133.0, 131.0, 130.4, 130.1, 129.6, 128.2 and 127.7 ppm.

Anal. Calcd. for $\text{C}_{15}\text{H}_9\text{Cl}_2\text{N}_3\text{S}_2$: C, 49.19; H, 2.48; N, 11.47. Found: C, 48.94; H, 2.62; N, 11.02.

1-(3-Chlorophenyl)-3-(4-chlorophenyl)-5-imino-2,4-imidazolidinedithione (**5p**).

This compound was prepared from *N*-(4-chlorophenyl)cyanothioformanilide and 3-chlorophenyl isothiocyanate similar to that of **5l**, mp 123-125°; ^{13}C nmr (deuteriochloroform): δ 179.9, 179.9, 156.1, 136.2, 135.1, 134.9, 133.5, 130.4, 129.9, 129.7, 129.2, 128.8 and 126.7 ppm; ir (dichloromethane): 3250, 1660, 1592 cm^{-1} .

Anal. Calcd. for $\text{C}_{15}\text{H}_9\text{Cl}_2\text{N}_3\text{S}_2$: C, 49.19; H, 2.48; N, 11.47. Found: C, 49.08, H, 2.75; N, 11.32.

1-(3-Chlorophenyl)-3-(2-methoxy-5-chlorophenyl)-5-imino-2,4-imidazolidinedithione (**5j1**).

Reaction conditions used for the preparation of **5j1** were similar to that of **3j1**, except for the reaction temperature. A solution of *N*-(2-methoxy-5-chlorophenyl)cyanothioformanilide **4j** (6.06 g), 3-chlorophenyl isothiocyanate (4.53 g), triethylamine (0.87 ml) and 95% ethanol (500 ml) was stirred at room temperature for 18 hours. The solution was then concentrated *in vacuo* to about 75 ml and a precipitate was formed. The resulting mixture was filtered to give 4.2 g (40%) of **5j1** having a melting point of 125° dec; ^{13}C nmr (deuteriochloroform): δ 179.5, 179.4, 156.2, 153.6, 135.0, 134.9, 131.6, 130.3, 129.8, 129.7, 128.8, 126.7, 125.6, 124.5, 113.6 and 56.3 ppm; ir (dichloromethane): 3240, 1650, 1582 cm^{-1} .

Anal. Calcd. for $\text{C}_{16}\text{H}_{11}\text{Cl}_2\text{N}_3\text{O}_2\text{S}_2$: C, 48.49; H, 2.80; N, 10.60. Found: C, 48.23; H, 2.83; N, 10.41.

1-(4-Methoxyphenyl)-3-(2-methoxy-5-chlorophenyl)-5-imino-2,4-imidazolidinedithione (**5j2**).

This compound was prepared from *N*-(2-methoxy-5-chlorophenyl)-

cyanothioformanilide and 4-methoxyphenyl isothiocyanate similar to that of **5j1**, mp 115-122°, 28% yield; ^{13}C nmr (deuteriochloroform): δ 180.1, 179.9, 160.1, 156.8, 153.6, 131.5, 129.8, 129.3, 126.9, 125.5, 124.6, 114.7, 113.6, 56.2 and 55.5 ppm; high resolution ms at m/e 391 (M^+): 391.0211 (Calcd. for $\text{C}_{17}\text{H}_{14}\text{ClN}_3\text{O}_2\text{S}_2$: 391.0217).

Anal. Calcd. for $\text{C}_{17}\text{H}_{14}\text{ClN}_3\text{O}_2\text{S}_2$: C, 52.10; H, 3.60; N, 10.72. Found: C, 51.88; H, 3.87; N, 10.31.

1-(2-Methyl-4-chlorophenyl)-3-(2-methoxy-5-chlorophenyl)-5-imino-2,4-imidazolidinedithione (**5j3**).

This compound was synthesized from *N*-(2-methoxy-5-chlorophenyl)cyanothioformanilide and 2-methyl, 4-chlorophenyl isothiocyanate similar to that of **5j1**, mp 178-181°, 71% yield; ^{13}C nmr (deuteriochloroform): δ 180.2, 179.3, 155.9, 153.4, 138.5, 136.0, 131.6, 131.5, 130.0, 129.8, 127.8, 127.7, 125.7, 118.6, 113.6, 56.3 and 17.5 ppm; ir (dichloromethane): 3240, 1655, 1596 cm^{-1} .

Anal. Calcd. for $\text{C}_{17}\text{H}_{13}\text{Cl}_2\text{N}_3\text{O}_2\text{S}_2$: C, 49.75; H, 3.19; N, 10.24. Found: C, 49.60; H, 3.21; N, 10.11.

1-(3-Chlorophenyl)-3-(2-methoxyphenyl)-5-imino-2,4-imidazolidinedithione (**5m**).

This compound was obtained from *N*-(2-methoxyphenyl)cyanothioformanilide **4m** and 3-chlorophenyl isothiocyanate in the presence of triethylamine at either 0° or ambient temperature, mp 148-151°; ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 180.3, 180.0, 155.6, 154.5, 135.6, 133.0, 131.5, 130.6, 129.7, 129.1, 128.7, 127.6, 123.6, 120.7, 112.8 and 55.9 ppm; ir (dichloromethane): 3250, 1660, 1590 cm^{-1} .

Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{ClN}_3\text{O}_2\text{S}_2$: C, 53.11; H, 3.34; N, 11.61. Found: C, 53.11; H, 3.67; N, 11.47.

1-(3-Chlorophenyl)-3-(2,4-dimethoxyphenyl)-5-imino-2,4-imidazolidinedithione (**5n**).

This compound was prepared from *N*-(2,4-dimethoxyphenyl)cyanothioformanilide and 3-chlorophenyl isothiocyanate similar to that of **5j1**, mp 185-187°; ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 180.6 (s), 180.3 (s), 161.6 (s), 155.6 (s), 155.4 (s), 135.7 (s), 132.9 (s), 130.6 (d), 130.2 (d), 129.0 (d), 128.7 (d), 127.6 (d), 116.4 (s), 105.5 (d), 99.4 (d), 55.9 (q) and 55.5 (q) ppm; ir (dichloromethane): 3240, 1655, 1600, 1590 cm^{-1} .

Anal. Calcd. for $\text{C}_{17}\text{H}_{14}\text{ClN}_3\text{O}_4\text{S}_2$: C, 52.10; H, 3.60; N, 10.72. Found: C, 51.91; H, 3.81; N, 10.61.

1-(3-Chlorophenyl)-3-(2,4,6-trimethylphenyl)-5-imino-2,4-imidazolidinedithione (**5o**).

This compound was prepared from *N*-(2,4,6-trimethylphenyl)cyno-

thioformanilide and 3-chlorophenyl isothiocyanate similar to that of **5j1**, mp 125-127°; ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 179.1, 179.1, 155.5, 139.2, 135.5, 135.4, 132.9, 130.5, 129.1, 129.0, 127.8, 20.6 and 17.2 ppm; ir (dichloromethane): 3240, 1660, 1592, 1585 cm^{-1} .

Anal. Calcd. for $\text{C}_{18}\text{H}_{16}\text{ClN}_3\text{S}_2$: C, 57.82; H, 4.31; N, 11.24. Found: C, 57.94; H, 4.48; N, 11.11.

Isomerization of Thiazolidinethione **3j1** to Imidazolidinedithione **5j1**.

A light yellow solution of thiazolidinethione **3j1** (500 mg) and 95% ethanol (400 ml) with 2 drops of triethylamine was stirred at room temperature for 18 hours. After removal of solvents *in vacuo*, ^{13}C nmr spectrum of the crude residue indicated the disappearance of **3j1** and the formation of its isomer **5j1**. The crude product was chromatographed on Florisil (100-200 mesh) using a hexane-ethyl acetate gradient elution to give 215 mg of imidazolidinedithione **5j1**. The ^{13}C nmr spectrum of this isolate was consistent with that of **5j1** prepared from *N*-(2-methoxy-5-chlorophenyl)cyanothioformanilide **4j** and 3-chlorophenyl isothiocyanate at room temperature.

Acknowledgements.

We would like to express our appreciation to H. Joyce [3], S. Singhawangcha [3] for many valuable discussions in the interpretation of the spectral data, to T. D. J. D'Silva for discussions during the preparation of this manuscript, and to E. C. Bailey for ^{13}C nmr spectra and D. S. Haigh for part of experimental work reported herein.

REFERENCES AND NOTES

- [#] Current address: Burroughs Wellcome Co., Research Triangle Park, North Carolina 27709.
- [1] I. Khattak, R. Ketcham, E. Schaumann and G. Adiwidjaja, *J. Org. Chem.*, **50**, 3431 (1985).
- [2] R. Ketcham and E. Schaumann, *J. Org. Chem.*, **45**, 3748 (1980).
- [3] Personal correspondence with Hobie Joyce (at the Union Carbide Co. Technical Center, South Charleston, WA) and S. Singhawangcha (Union Carbide Agricultural Products Co., Research Triangle Park, NC) in 1983.
- [4] High resolution ms at m/e 365: 364.9611 (Calcd. for $\text{C}_{15}\text{H}_9\text{Cl}_2\text{N}_3\text{S}_2$: 364.9616). At m/e 288: 288.0099 (Calcd. for $\text{C}_{14}\text{H}_8\text{Cl}_2\text{N}_3$: 288.0096).
- [5] The chemical shift pattern of these imidazolidinedithiones agrees well with that reported on 1,3-diphenyl-5-imino-2,4-imidazolidinedithione **1** (δ 180.3, 180.2 and 156.4 ppm) in Reference No. 1.
- [6] B. Kumelj and M. Tisler, *Vestnik sloven. kemi. rdustva*, **5**, 69 (1958); *Chem. Abstr.*, **54**, 22426f (1960).