Reactions of 5-(Arylimino)-4-chloro-5*H*-1,2,3-dithiazoles with Primary and Secondary Alkylamines: Novel Synthesis of (Arylimino)cyanomethyl Alkylamino Disulfides and Their Mechanisms of Formation

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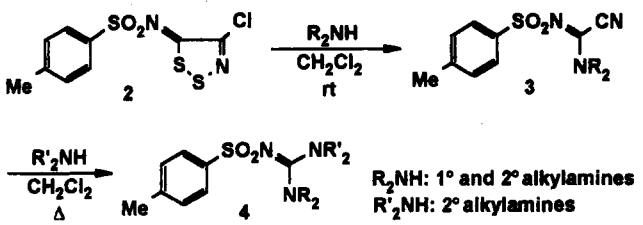
Reactions of 5-(arylimino)-4-chloro-5*H*-1,2,3-dithiazoles with alkylamines such as isopropylamine, piperidine, pyrrolidine, and diethylamine in methylene chloride at room temperature gave (arylimino)-cyanomethyl alkylamino disulfides (14–83%) along with *N'*-aryl-*N*-alkylcyanoformamidines (0–88%). The yields of the latter increase and those of the former decrease with the concentration of the amine. In addition, some of the latter compounds were independently synthesized by treatment of the former with cyclic amines such as piperidine, pyrrolidine, and morpholine in methylene chloride at room temperature (22–97%). The results indicate that the former compounds are involved as intermediates in the formation of the latter in these reactions. However, when [(*p*-nitrophenyl)-imino]cyanomethyl (pentane-1,5-diyl)amino disulfide was treated with sterically bulky amines such as *tert*-butyl- and diethylamines at reflux and room temperature, respectively, cyanoformamidines having a piperidine moiety rather than *tert*-butyl- and diethylamino groups were obtained as the only isolable products. Two pathways which involve initially either direct nucleophilic attack of alkylamines on the imino carbon or on the sulfur α to the amino group of (arylimino)cyanomethyl alkylamino disulfides are proposed to rationalize the results.

Introduction

5-(Arylimino)-4-chloro-5*H*-1,2,3-dithiazoles (1), which were prepared by the reaction of 4,5-dichloro-1,2,3-dithiazolium chloride with primary arylamines in methylene chloride in the presence of pyridine at room temperature,[1] are an interesting class of heterocyclic compounds not only because of their usefulness as acaricides[2] and herbicides[2,3] but also because of their potential utility as synthetic intermediates.[1,4-6] However, analogous reactions with primary alkylamines were reported to be complicated and only two products were identified.[1] Surprisingly, heating of 4-chloro-5-[(*p*-tolylsulfonyl)imino]-5*H*-1,2,3-dithiazole (2) in DMF for 30 min at reflux gave *N'*-(*p*-tolylsulfonyl)-*N,N*-dimethylcyanoformamidine (3) (R = Me) in 64% yield. This result led us to investigate the reactions of 2 with various primary and secondary alkylamines which resulted in our reporting a new general synthetic method for *N'*-(*p*-tolylsulfonyl)-*N*-alkyl- and *N,N*-dialkylcyanoformamidines (3) and 1,3-dialkyl-2-(*p*-tolylsulfonyl)guanidines (4)[4] as shown in Scheme I.

The reactions were the first examples with a sulfonyl group at the imino nitrogen atom of cyanoformamidines and guanidines. Although synthesis of *N'*-aryl-*N*-alkylcyanoformamidines has been reported[7] and various sulfamoyl guanidines were prepared from the aminolysis of the *N,N*-dialkyl-*N*-(chlorosulfonyl)chloroformamidines

Scheme I



with primary or secondary amines,[8] compounds 3 and 4 cannot be prepared by that method. The mechanism of formation of the cyanoformamidines 3 is, however, uncertain. One might envisage the direct nucleophilic attack of an amine on the imino carbon atom of 2 (path a, Scheme II), followed by elimination of S_2 along with hydrogen chloride to give cyanoformamidine 3[9] (path a, Scheme II). Formation of the nitrilium ion 5, followed by nucleophilic attack of the amine to give 3 (path b, Scheme II) might be considered as in the proposed mechanism for the thermolysis of 1c.[5] However, it is unlikely on the following grounds: too low a reaction temperature performed (25 °C) and the instability of the nitrilium ion 5, which has an electron-deficient center adjacent to a sulfonyl group known to be a strong electron-withdrawing group. On the other hand, nucleophilic attack of an amine on the sulfur atom at the position 2 to give (*p*-tosylimino)cyanomethyl alkylamino disulfides (6) (path c, Scheme II), followed by nucleophilic attack of another molecule of the amine on the imino carbon of 6 might also give 3 after eliminations of sulfur and the amine bonded to sulfur as shown in Scheme II.

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(9) The mechanism of formation of 3-cyanobenzoxazole from thermolysis of 4-chloro-5-[(*o*-hydroxyphenyl)imino]-5*H*-1,2,3-dithiazole was proposed by intramolecular nucleophilic attack of the hydroxy group on the imino carbon, followed by elimination of S_2 and chloride ion. Refer to ref 5.

0022-3263/93/1958-7001$04.00/0

Scheme II

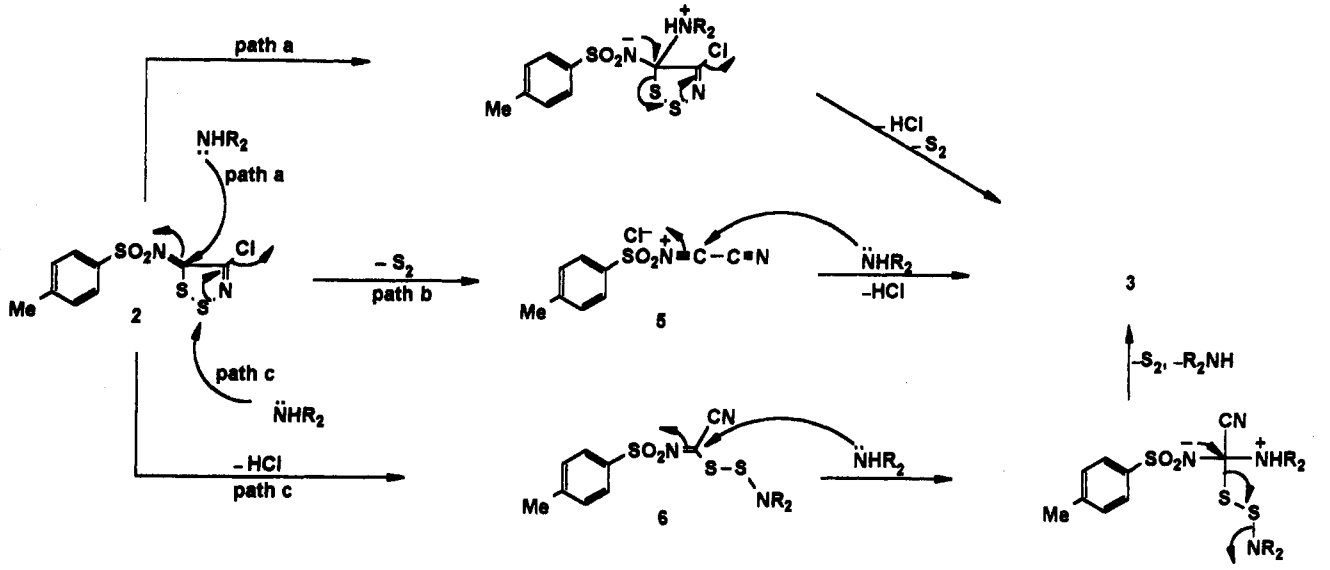
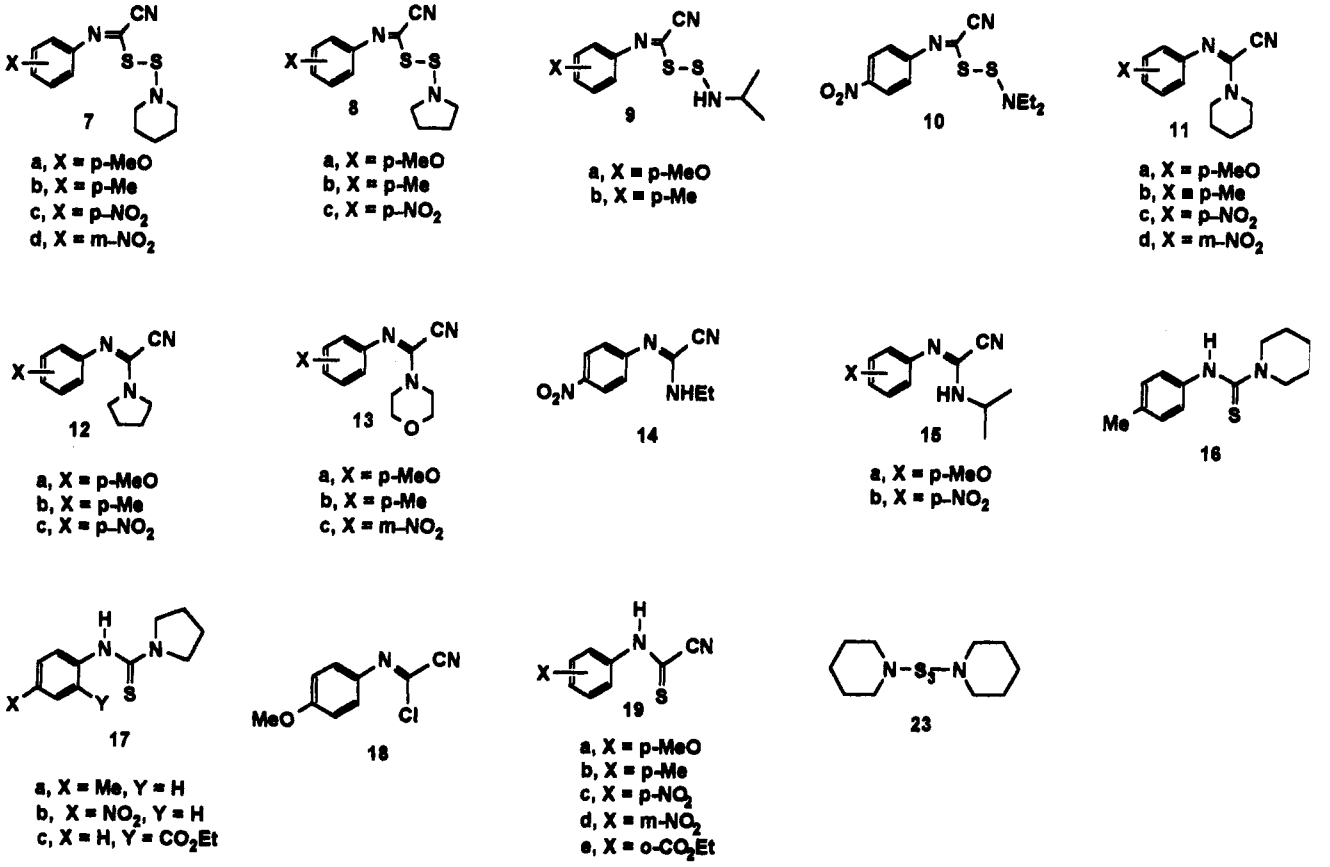


Chart I



a, X = p-MeO
b, X = p-Me
c, X = p-NO_2
d, X = m-NO_2

a, X = p-MeO
b, X = p-Me
c, X = p-NO_2

a, X = p-MeO
b, X = p-Me

a, X = p-MeO
b, X = p-Me
c, X = p-NO_2
d, X = m-NO_2

a, X = p-MeO
b, X = p-Me
c, X = p-NO_2

a, X = p-MeO
b, X = p-Me
c, X = m-NO_2

a, X = p-MeO
b, X = p-NO_2

a, X = Me, Y = H
b, X = NO_2, Y = H
c, X = H, Y = CO_2Et

a, X = p-MeO
b, X = p-Me
c, X = p-NO_2
d, X = m-NO_2
e, X = o-CO_2Et

In order to obtain the mechanistic information on the cleavage of dithiazole ring by alkylamines, reactions of 2 with a variety of primary and secondary alkylamines were investigated at room temperature. However, the major products were always cyanoformamidines 3 and/or guanidine derivatives 4 depending on the nature of the alkylamines. No compound of the type 6 was isolated. Therefore, we have studied the reactions of 1 with primary and secondary alkylamines under the various conditions. The results are described herein.

Results and Discussion

The reactions of 5-(*p*-anisylimino)-4-chloro-5*H*-1,2,3-dithiazole (**1a**) with 2 equiv of piperidine in methylene chloride at room temperature afforded (*p*-anisylimino)-cyanomethyl (pentane-1,5-diyl)amino disulfide (**7a**) and *N'*-(*p*-anisyl)-*N*,*N*-(pentane-1,5-diyl)cyanoformamidine (**11a**) in 53 and 32% yields, respectively. Treatment of **1a** with 2 equiv of pyrrolidine under the same conditions afforded (*p*-anisylimino)cyanomethyl (butane-1,4-diyl)-amino disulfide (**8a**) in 65% yield. No *N'*-(*p*-anisyl)-*N*,*N*-(butane-1,4-diyl)cyanoformamidine (**12a**) was detected. When 3.8 equiv of pyrrolidine was used, **12a** was obtained in 88% yield. Similar treatment of **1a** with 2 equiv of isopropylamine, however, afforded (*p*-anisylimino)cyanomethyl isopropylamino disulfide (**9a**) in 14% yield along with the recovery of **1a** in 55% yield. On the other hand, the reaction of **1a** with 2 equiv of morpholine under the

Table I. Reactions of 5-(*p*-Anisylimino)-4-chloro-5*H*-1,2,3-dithiazole (1a) with Primary and Secondary Alkylamines

entry	1a (mM)	amine (mM)	reaction time, h	yield[a] (%) 1a	disulfide	amidine
1	1.95	piperidine (4.0)	1.5		**7a** (53)	**11a** (32)
2	2.08	pyrrolidine (4.2)	1.5		**8a** (65)	
3	1.25	pyrrolidine (4.8)	1.0			**12a** (88)
4	3.86	isopropylamine (7.8)	1.5	55	**9a** (14)	
5	1.97	morpholine (4.0)	1.5	50		**13a** (23)
6	1.02	morpholine (4.6)	1.0			**13a** (87)

[a] Isolated yields.

Table II. Reactions of 4-Chloro-5-(*p*-tolylimino)-5*H*-1,2,3-dithiazole (1b) with Primary and Secondary Alkylamines

entry	1b (mM)	amine (mM)	reaction time, h	yield[a] (%) 1b	disulfide	amidine
1	1.08	piperidine (2.4)	1.0		**7b** (64)	
2	2.06	piperidine (6.1)	1.0			**11b** (49)[b]
3	0.869	pyrrolidine (1.8)	1.5	8	**8b** (56)	**12b** (18)
4	2.07	pyrrolidine (6.0)	0.5			**12b** (84)[c]
5	1.31	isopropylamine (2.9)	1.5	49	**9b** (23)	
6	2.31	morpholine (6.8)	2.5			**13b** (77)

[a] Isolated yields. [b] *N,N*-(Pentane-1,5-diyl)-*N'*-(*p*-tolyl)thiourea (16) (9%) and an unknown compound were isolated. [c] *N,N*-(Butane-1,4-diyl)-*N'*-(*p*-tolyl)thiourea (**17a**) (12%) was isolated.

Table III. Reactions of 4-Chloro-5-[(*p*-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (1c) with Primary and Secondary Alkylamines

entry	1c (mM)	amine (mM)	reaction time, h	yield[a] (%) 1c	disulfide	amidine
1	1.97	piperidine (4.0)	0.5	15	**7c** (83)	
2	1.85	piperidine (7.6)	12			**11c** (47)
3	0.902	pyrrolidine (2.0)	0.5		**8c** (47)	**12c** (18)
4	1.87	diethylamine (3.8)	1.0		**10** (36)	
5	2.02	ethylamine (16)	15			**14** (48)
6	1.08	isopropylamine (2.3)	1.5	47		
7	3.57	*tert*-butylamine (14)	2.0	14		

[a] Isolated yields.

Table IV. Reactions of 4-Chloro-5-[(*m*-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (1d) with Piperidine

entry	1d (mM)	piperidine (mM)	reaction time, h	yield[a] (%) 1d	disulfide	amidine
1	0.773	1.7	0.5	16	**7d** (80)	
2	2.19	8.7	4.0			**11d** (14)
3	1.71	10	30			**11d** (26)

[a] Isolated yields.

same conditions gave no amino iminomethyl disulfide. Instead, *N'*-(*p*-anisyl)-*N,N*-(3-oxapentane-1,5-diyl)cyanoformamidine (**13a**) and **1a** were isolated in 23 and 50% yields, respectively. When 4.5 equiv of morpholine was used, **13a** was isolated in 86% yield. The reactions of 4-chloro-5-(*p*-tolylimino)- (**1b**), 4-chloro-5-[(*p*-nitrophenyl)imino]- (**1c**), and 4-chloro-5-[(*m*-nitrophenyl)imino]-5*H*-1,2,3-dithiazoles (**1d**) with alkylamines which were used for the reaction of **1a** proceeded in the similar manner under the same conditions. The results are summarized in Table I–IV.

The strucutres of amino iminomethyl disulfides **7–10** and cyanoformamidines **11–14** were assigned on the basis of the spectroscopic data and microanalyses. To our knowledge, the amino iminomethyl disulfides **7–10** have never been reported. Moreover, the isolation of the compounds **7–10** are indeed the first evidence for the mechanistic suggestion that nucleophiles might attack the sulfur atom at the position 2 among the possible nucleophilic centers, S-1, S-2, C-4, and C-5 of aromatic 1,2,3-dithiazole derivatives **1**. When 2 equiv of alkylamines were used, the major product of each reaction was amino iminomethyl disulfide **7–10** (14–83%) except for the reactions with isopropylamine and morpholine. From the reactions of **1a**, **1b**, and **1c** with 2 equiv of isopropylamine were recovered **1a**, **1b**, and **1c** in 55% (Table I, entry 4), 49% (Table II, entry 5), and 47% (Table III, entry 6) yields and the amino iminomethyl disulfides **9a** and **9b** were isolated as minor products from the reactions of **1a** and **1b** in 14% (Table I, entry 4) and 23% (Table II, entry 5) yields, respectively. However, no amino iminomethyl disulfide was isolated from the reaction of **1c** (Table III, entry 6). The recovery of approximately half of the starting material might be due to the steric hindrance by the bulky isopropyl group. The fact that the reaction of **1c** with 4 equiv of *tert*-butylamine did not afford the amino iminomethyl disulfide can be explained on the same ground (Table III, entry 7).

On the other hand, the reactions of either **1a** or **1b** with morpholine did not give the corresponding amino iminomethyl disulfide. Cyanoformamidines **13a** and **13b** were isolated, respectively (Table I, entries 5, 6; Table II, entry 6).

The reaction of **1c** with an excess of ethylamine also gave *N'*-(*p*-nitrophenyl)-*N*-ethylcyanoformamidine (**14**), whereas the same reaction with diethylamine afforded the amino iminomethyl disulfide **10** without the formation of the corresponding cyanoformamidine (Table III, entries 4, 5). The failure for even the detection of the corresponding amino iminomethyl disulfides in the reactions of **1a** and **1b** with morpholine or in the reaction with ethylamine might be due to the rapid transformation of the amino iminomethyl disulfides into the cyanoformamidines by the nucleophilic attack of the amines present in excess. This view is supported by the results in which more than 2 equiv of cyclic amines are used; the yields of cyanoformamidines increase at the expense of those of the corresponding amino iminomethyl disulfides.

To confirm the intermediacy of the amino iminomethyl disulfides during the course of the formation of cyanoformamidines, the selected compounds **7a**, **7c**, and **7d** were treated with primary and secondary alkylamines in methylene chloride either at room or reflux temperature. From the reactions were isolated the expected cyanoformamidines, the yields of which depended on the substituent on *N*-aryl group of the amino iminomethyl disulfides **7a**, **7c**, and **7d** and the structures of the amines used. The results are summarized in Table V.

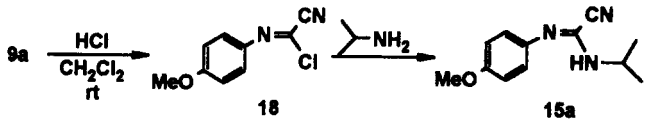
The reactions of **7a** with a large excess of pyrrolidine at room temperature proceeded smoothly to give cyanoformamidine **12a** in excellent yield (Table V, entry 1), whereas the reaction with isopropylamine under the same conditions did not proceed at room temperature. Surprisingly, *N'*-(*p*-anisyl)-*N,N*-(pentane-1,5-diyl)cyanoformamidine (**11a**) was obtained in 26% yield at reflux (Table V, entry 2). The compound **11a** ought to have been formed by the reaction of **7a** with piperidine. The expected compound, *N'*-(*p*-anisyl)-*N*-isopropylcyanoformamidine (**15a**), however, was prepared from the reaction of isopropylamine

Table V. Preparation of *N'*-Aryl-*N*-alkylcyanoformamidines from (Arylimino)cyanomethyl *N,N*-(Pentane-1,5-diyl)amino Disulfides (7a, 7c, 7d)

entry	compound (mM)	amine (mM)	reaction time, h	reaction temp	yield[a] (%) amidine
1	**7a** (0.163)	pyrrolidine (1.2)	1.5	rt	**12a** (97)
2	**7a** (0.621)	isopropylamine (4.7)	3.0	reflux	**11a** (26)
3	**7c** (1.80)	piperidine (5.6)	12	rt	**11c** (43)
4	**7c** (0.822)	pyrrolidine (6.0)	1.5	rt	**12c** (24)[b]
5	**7c** (1.12)	ethylamine (13)	15	rt	**14** (25), **11c** (5)
6	**7c** (0.372)	isopropylamine (4.7)	5.0	reflux	**15b** (45), **11c** (44)
7	**7c** (0.828)	*tert*-butylamine (7.5)	5.0	reflux	**11c** (49)
8	**7c** (1.52)	diethylamine (5.8)	24	rt	**11c** (22)
9	**7d** (0.599)	piperidine (3.0)	30	rt	**11d** (22)
10	**7d** (1.46)	morpholine (8.1)	0.5	rt	**13c** (77)

[a] Isolated yields. [b] *N,N*-(Butane-1,4-diyl)-*N'*-(*p*-nitrophenyl)thiourea (**17b**) was isolated in 48% yield.

Scheme III



with *N*-(*p*-anisyl)cyanoimidoyl chloride (**18**) in 97% yield as shown in Scheme III.

In the meantime, the reaction of **7c** with 3 equiv of piperidine and 7 equiv of pyrrolidine under the similar conditions as with **7a**, afforded *N'*-(*p*-nitrophenyl)-*N,N*-(pentane-1,5-diyl)cyanoformamidine (**11c**) and *N'*-(*p*-nitrophenyl)-*N,N*-(butane-1,4-diyl)cyanoformamidine (**12c**), respectively, as expected (Table V, entries 3, 4). Noteworthy observation was the isolation of a thiourea derivative **17b** from the reaction with pyrrolidine (Table V, entry 4).

Reaction of **7c** with ethylamine at room temperature afforded the cyanoformamidine **14** in 25% yield concomitant with **11c** in 5% yield. The latter should be formed by the reaction of **7c** with piperidine. The yield of **11c** increased to 44, 49, and 22% when **7c** was reacted with isopropyl- and *tert*-butylamines at reflux and diethylamine at room temperature, respectively (Table V, entries 6, 7, 8). In particular, the reaction with *tert*-butylamine, which is much bulkier than isopropylamine, did not afford the expected cyanoformamidine having a *tert*-butyl group at all (Table V, entry 7). The reaction with diethylamine, which is bulkier than ethylamine, gave **11c** at room temperature in 22% yield together with complex mixtures (Table V, entry 8). It is interesting to compare at this juncture the result obtained from the reaction with a cyclic amine, pyrrolidine (Table V, entry 4), with that of the reaction with the corresponding acyclic amine, diethylamine (Table V, entry 8). It has been known that pyrrolidine is a stronger nucleophile than diethylamine simply because the former has a pair of extruded electrons on nitrogen whereas the latter has the corresponding electrons which are shielded substantially by the two floppy ethyl groups. Hence, it is to be expected that the sterically less-hindered pyrrolidine reacts with **7c** to give the expected cyanoformamidine **12c** and the reaction with the sterically more-bulky diethylamine does not give the cyanoformamidine having a diethyl group.

The reaction of **7d** with piperidine proceeded smoothly at room temperature to give *N'*-(*m*-nitrophenyl)-*N,N*-(pentane-1,5-diyl)cyanoformamidine (**11d**) as in the reaction of **1d** with the same amine (Table IV, entries 2,3), albeit in low yields. A similar result was obtained from the reaction of **7d** with morpholine (Table V, entry 10).

The results indicate that the amino iminomethyl disulfides of the type **7** can act as intermediates in the course of the formation of cyanoformamidines. The mechanisms of the reaction of **1** with alkylamines proposed are outlined in Scheme IV.

Nucleophilic attack of piperidine at S-2 of 5-(arylimino)-4-chloro-5*H*-1,2,3-dithiazoles (**1**) followed by elimination of hydrogen chloride affords (arylimino)cyanomethyl (pentane-1,5-diyl)amino disulfides **7**, which are attacked by alkylamines in two ways depending on the steric bulkiness of the amines. Cyclic amines with a pair of protruded electrons such as pyrrolidine, piperidine, and morpholine attack directly at the imino carbon of the amino iminomethyl disulfides **7** followed by eliminations of sulfur and piperidine in a concerted manner to give cyanoformamidines (**11–15**) (path a). Whereas, the sterically hindered amine such as *tert*-butylamine might attack at the sulfur atom α to the nitrogen atom of the piperidine ring to give *N*-arylcyanothioformamides **19** and bisamino sulfides **20**, which decompose to generate piperidine (path b). The piperidine generated by path b is in turn involved in the formation of cyanoformamidine **11c** according to path a. Although no *N*-arylcyanothioformamides **19** could be isolated during the course of these reactions, the assumption that the compounds **19** are involved as intermediates is very useful to explain the mechanism of formation of thiourea derivatives in the reaction of **7c** with pyrrolidine (Table V, entry 4) as well as in the reaction of **1b** with piperidine or pyrrolidine (Table II, entries 2, 4). That is, elimination of hydrogen cyanide from **19** by an amine present in excess yields aryl isothiocyanates **21**, and further reaction of **21** with the amine resulting in thiourea derivatives **16** and **17**. Alternatively, addition of the amine to *N*-arylcyanothioformamide **19** gives the intermediate **22**, which can eliminate either hydrogen cyanide to give eventually thiourea derivatives **16** and **17** or hydrogen sulfide to give cyanoformamidines **11b**, **12b**, and **12c**.

N-Arylcyanothioformamides **19** are good dipolarophiles[10] and are useful in the synthesis of a variety of heterocyclic compounds.[10d,e,11] It has been reported that treatment of **19** (X = *o*-Cl, *o*-Br, *p*-I) with ammonia gas, followed by hydrogen sulfide in ethanol gave *N*-aryldithiooxamides.[12] However, no study with amines has appeared in the literature. In order to ascertain the stability of *N*-arylcyanothioformamides **19**, compounds **19a**, **19c**, and **19e** were treated with alkylamines. The results are summarized in Table VI.

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(11) Kumelj, B.; Tisler, M. *Vestn. Slov. kem. Drust.* **1958**, *5*, 69. *Chem. Abstr.* **1960**, *54*, 22426f.

(12) Grabenko, A. D.; Pel'kis, P. S. *Zhur. Obshchei Khim.* **1961**, *30*, 1222. *Chem. Abstr.* **1961**, *55*, 1484f.

Scheme IV

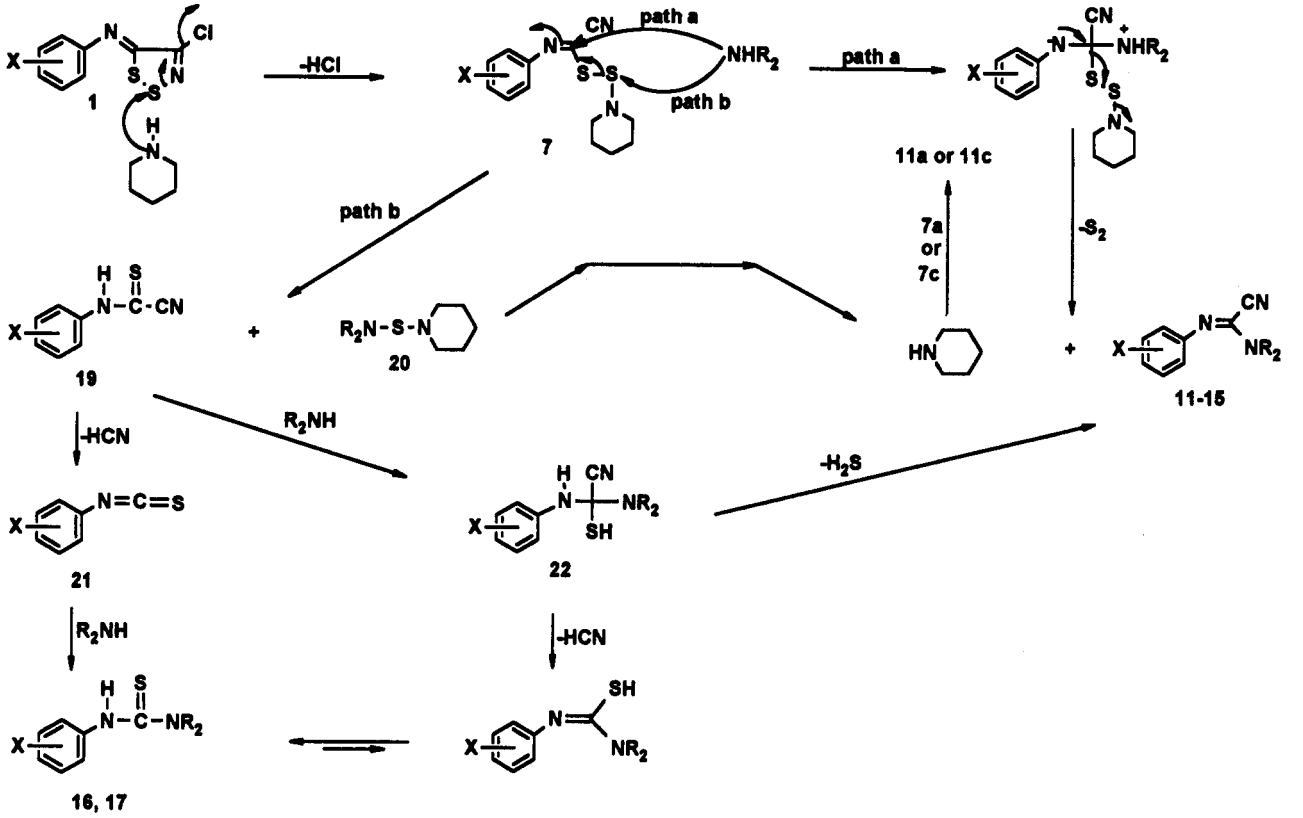

Table VI. Reactions of *N*-Arylcyanothioformamides (19a, 19c, 19e) with Alkylamines

entry	compound (mM)	amine (mM)	reaction time, min	reaction temp	yield[a] (%) amidine	yield[a] (%) thiourea
1	**19a** (0.624)	pyrrolidine (3.0)	10	rt	**12a** (66)	
2	**19c** (1.06)	piperidine (2.0)	30	reflux	*b*	
3	**19c** (1.07)	isopropylamine (3.5)	10	rt	*b*	
4	**19c** (0.444)	*tert*-butylamine (1.9)	10	rt	*b*	
5	**19c** (0.874)	pyrrolidine (4.2)	10	rt	**12c** (14)	**17b** (39)
6	**19e** (0.862)	pyrrolidine (4.8)	5	rt		**17c** (95)

[a] Isolated yields. [b] Unidentifiable complex mixtures.

The reaction of **19c** with 2 equiv of piperidine resulted in a complex mixture of products from which only two compounds whose structures have not been determined could be isolated. Similar treatment of **19c** with either isopropyl- or *tert*-butylamine at room temperature afforded complex mixtures, too. On the other hand, the reaction of **19c** with pyrrolidine at room temperature afforded the cyanoformamidine **12c** and a thiourea derivative **17b** in 14 and 39% yields, respectively. The reaction of **19a** with pyrrolidine under the same condition as with **19c** afforded only the corresponding cyanoformamidine **12a** in 66% yield. Similar reaction of **19e** with pyrrolidine, however, afforded only the thiourea derivative **17c** in 95% yield. These results indicate that either cyanoformamides or thioureas or both can be formed from the reactions of *N*-arylcyanothioformamides **19** with alkylamines depending on the *N*-aryl group substituent of **19** and the alkylamines as proposed in Scheme IV. However, further details of the reactions should be investigated.

Attempts to isolate bisamino sulfides **20**, which were presumably formed from the reactions of **1** or **7** with alkylamines according to path b, failed. Instead, bis(piperidino)trisulfide (**23**) was isolated as shown in Table VII.

Table VII. Yields of Bis(piperidino) Trisulfide (23) Isolated from the Reaction of 1c, 1d, 7c, and 7d with Piperidine

compound (mM)	piperidine (mM)	yield[a] (%) **23**
1c (1.85)	7.6	62
1d (1.71)	10	43
7c (1.80)	5.6	61
7d (0.599)	3.0	26

[a] Isolated yields.

The structure of **23** was determined based on the spectroscopic and mass spectral data and by comparison of its melting point with that reported in the literature.[13] Since bis(dialkylamino) sulfides such as bis(diethylamino) sulfide and bis(dimethylamino) sulfide are reported to be more sensitive to moisture than bis[(4-oxapentane-1,5-diyl)amino] sulfide,[14] and furthermore, unsymmetrical bis(dialkylamino) sulfides are known to undergo ready disproportionation reactions to give the symmetrical counterparts,[15] it is expected that the unsymmetrical bis(dialkylamino) sulfides **20** are unstable enough to undergo decomposition. In fact, the reactions of either **1** or amino

(13) Levi, T. G. *Gazz. Chim. Ital.* **1931**, *61*, 286. *Chem. Abstr.* **1931**, *25*, 4853.
(14) Kutateladze, G.; Kice, J. L.; Kutateladze, A. G.; Zefirov, N. S.; Zuk, N. V. *J. Org. Chem.* **1991**, *56*, 5235.
(15) Harpp, D. N.; Back, T. G. *Tetrahedron Lett* **1972**, 1481.

iminomethyl disulfides 7–11 with alkylamines gave always mixtures corresponding to bisamino sulfides, R_2N-S_x-NR'_2 (x = 1, 2, 3, etc.) according to ^{1}H NMR and mass spectral data. The separation of the mixtures by either column chromatography or HPLC was occasionally successful in the cases listed in Table VII. At present it is rather difficult to elucidate the fate of **20** under the reaction conditions.

Experimental Section

The ^{1}H NMR spectra were recorded at 60 MHz in $CDCl_3$ solution containing Me_4Si as an internal standard, unless otherwise specified. IR spectra were recorded in KBr or thin films on KBr plates. HPLC was performed using Waters Model 510 equipped with a C-18 column (μBondapak C18, 10 μm, 7.8 × 300 mm i.d.) and differential refractometer, using CH_3CN as eluant (flow rate = 0.8 mL/min). Mass spectra were obtained on a Varian Mat 711. Elemental analyses were determined by Korea Basic Science Center. Column chromatography was performed using silica gel (70–230 mesh, Merck). Melting points are uncorrected.

5-(Arylimino)-4-chloro-5*H*-1,2,3-dithiazoles (1). Dithiazoles **1** were prepared by the literature method.[1]

5-(*p*-Anisylimino)-4-chloro-5*H*-1,2,3-dithiazole (1a): mp 86–88 °C (lit.[1] mp 89 °C).

4-(Chloro-5-[(*p*-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (1c): mp 166–168 °C (lit.[1] mp 160 °C).

4-Chloro-5-(*p*-tolylimino)-5*H*-1,2,3-dithiazole (1b): mp 71–72 °C; ^{1}H NMR δ 2.42 (s, 3H, Me), 7.24 (s, 4H, Ar); IR (KBr) 1580, 1570, 1500, 1220, 1137, 860, 818, 790, 758 cm^{-1}; MS (*m*/*z*) 242 (M$^+$). Anal. Calcd for $C_9H_7ClN_2S_2$: C, 44.53; H, 2.19; N, 11.54; S, 26.42. Found: C, 44.33; H, 2.11; N, 11.47; S, 27.01.

4-Chloro-5-[(*m*-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (1d): mp 125.5–126 °C; ^{1}H NMR δ 7.48–7.86 (m, 2H, Ar), 8.00–8.25 (m, 2H, Ar); IR (KBr) 1585, 1510, 1355, 1225, 1150, 896, 868, 828, 800, 781, 738, 705, 680 cm^{-1}; MS (*m*/*z*) 273 (M$^+$). Anal. Calcd for $C_8H_4ClN_3O_2S_2$: C, 35.11; H, 1.47; N, 15.35; S, 23.43. Found: C, 35.05; H, 1.43; N, 15.21; S, 24.35.

5-[(*o*-Carbethoxyphenyl)imino]-4-chloro-5*H*-1,2,3-dithiazole (1e): ^{1}H NMR δ 1.35 (t, J = 7 Hz, 3H, Me), 4.35 (q, J = 7 Hz, 2H, OCH_2), 6.95–7.86 (m, 4H, Ar); IR (neat) 1708 (C=O), 1590, 1471, 1440, 1386, 1290, 1246, 1215, 1150, 1130, 1080, 857, 760, 705, 675 cm^{-1}; MS (*m*/*z*) 300 (M$^+$). Anal. Calcd for $C_{11}H_9ClN_2O_2S_2$: C, 43.93; H, 3.02; N, 9.31; S, 21.32. Found: C, 43.83; H, 3.00; N, 9.30; S, 22.42.

General Procedure for the Reactions of 1 with Alkylamines. To a solution of **1** in CH_2Cl_2 was added an excess amount of an alkylamine, which was stirred for an appropriate time at either room temperature or reflux temperature (refer to Table I–IV). After removal of the solvent under vacuo, the residue was chromatographed on a silica gel column (1.0 × 15 cm) using a series of the solvents. The bp of petroleum ether used was 30–70 °C.

(*p*-Anisylimino)cyanomethyl (Pentane-1,5-diyl)amino Disulfide (7a). The reaction of 506 mg (1.95 mmol) of 5-(*p*-anisylimino)-4-chloro-5*H*-1,2,3-dithiazole (**1a**) with 0.40 mL (4.0 mmol) of piperidine in 30 mL of CH_2Cl_2, followed by chromatography using a mixture of petroleum ether and CH_2Cl_2 (1:3) afforded 465 mg of a crude compound **7a**, which was analyzed on HPLC yielding 320 mg (1.04 mmol, 53%) of **7a**. The compound **7a** was recrystallized from *n*-hexane, mp 66–67 °C; ^{1}H NMR δ 1.32–1.93 (m, 6H, $3CH_2$), 2.75–3.26 (m, 4H, CH_2NCH_2), 3.83 (s, 3H, OMe), 6.80–7.47 (m, 4H, Ar); IR (neat) 2225 (C≡N) cm^{-1}; MS (*m*/*z*) 307 (M$^+$). Anal. Calcd for $C_{14}H_{17}N_3OS_2$: C, 54.70; H, 5.57; N, 13.67; S, 20.86. Found: C, 54.52; H, 5.49; N, 13.70; S, 21.32. Elution next with CH_2Cl_2 gave 23 mg of a mixture of unknown compounds and 152 mg (0.624 mmol, 32%) of *N'*-(*p*-anisyl)-*N*,*N*-(pentane-1,5-diyl)cyanoformamidine (**11a**) as a liquid: ^{1}H NMR δ 1.60–1.90 (m, 6H, $3CH_2$), 3.50–3.95 (m, 7H, OMe, CH_2NCH_2), 6.95 (s, 4H, Ar); IR (neat) 2226 (C≡N) cm^{-1}; MS (*m*/*z*) 243 (M$^+$). Anal. Calcd for $C_{14}H_{17}N_3O$: C, 69.11; H, 7.04; N, 17.27. Found: C, 69.10; H, 6.99; N, 17.30.

(*p*-Tolylimino)cyanomethyl (Pentane-1,5-diyl)amino Disulfide (7b). The reaction of 262 mg (1.08 mmol) of 4-chloro-5-(*p*-tolylimino)-5*H*-1,2,3-dithiazole (**1b**) with 0.24 mL (2.4 mmol) of piperidine in 30 mL of CH_2Cl_2, followed by chromatography using a mixture of petroleum ether and CH_2Cl_2 (1:3), gave 276 mg of a mixture, which was analyzed on HPLC yielding 201 mg (0.690 mmol, 64%) of **7b** as a liquid: ^{1}H NMR δ 1.10–1.95 (m, 6H, $3CH_2$), 2.40 (s, 3H, Me), 2.80–3.33 (m, 4H, CH_2NCH_2), 6.97–7.50 (m, 4H, Ar); IR (neat) 2220 (C≡N) cm^{-1}; MS (*m*/*z*) 291 (M$^+$). Anal. Calcd for $C_{14}H_{17}N_3S_2$: C, 57.70; H, 5.88; N, 14.42; S, 22.00. Found: C, 57.53; H, 5.75; N, 14.23; S, 22.49.

(*p*-Nitrophenylimino)cyanomethyl (Pentane-1,5-diyl)amino Disulfide (7c). The reaction of 539 mg (1.97 mmol) of 4-chloro-5-[(*p*-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (**1c**) with 0.40 mL (4.0 mmol) of piperidine in 50 mL of CH_2Cl_2, followed by chromatography using CH_2Cl_2 afforded 625 mg of a mixture, which was recrystallized from a mixture of $CHCl_3$ and *n*-hexane to give 82 mg (0.302 mmol, 15%) of **1c**. Concentration of the filtrate, followed by recrystallization from *n*-hexane gave 525 mg (1.64 mmol, 83%) of **7c**: mp 76–77 °C; ^{1}H NMR δ 1.05–2.10 (m, 6H, $3CH_2$), 2.85–3.33 (m, 4H, CH_2NCH_2), 7.02–7.42 (m, 2H, Ar), 8.42 (d, J = 9 H, 2H, Ar); IR (neat) 2220 (C≡N) cm^{-1}; MS (*m*/*z*) 322 (M$^+$). Anal. Calcd for $C_{13}H_{14}N_4O_2S_2$: C, 48.43; H, 4.38; N, 17.38; S, 19.89. Found: C, 48.21; H, 4.35; N, 17.40; S, 20.31.

[(*m*-Nitrophenyl)imino]cyanomethyl (Pentane-1,5-diyl)amino Disulfide (7d). The reaction of 212 mg (0.773 mmol) of 4-chloro-5-[(*m*-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (**1d**) with 0.17 mL (1.7 mmol) of piperidine in 20 mL of CH_2Cl_2, followed by chromatography using CH_2Cl_2, afforded 244 mg of a mixture, which was analyzed on HPLC yielding 33 mg (0.121 mmol, 16%) of **1d**, and 200 mg (0.620 mmol, 80%) of **7d** which was recrystallized from *n*-hexane; mp 46–47 °C; ^{1}H NMR δ 1.13–2.06 (m, 6H, $3CH_2$), 2.75–3.40 (m, 4H, CH_2NCH_2), 7.26–8.45 (m, 4H, Ar); IR (neat) 2220 (C≡N) cm^{-1}; MS (*m*/*z*) 322 (M$^+$). Anal. Calcd for $C_{13}H_{14}N_4O_2S_2$: C, 48.43; H, 4.38; N, 17.38; S, 19.89. Found: C, 48.25; H, 4.30; N, 17.37; S, 20.40.

(*p*-Anisylimino)cyanomethyl (Butane-1,4-diyl)amino Disulfide (8a). The reaction of 537 mg (2.08 mmol) of **1a** with 0.35 mL (4.2 mmol) of pyrrolidine in 30 mL of CH_2Cl_2, followed by chromatography using a mixture of petroleum ether and CH_2Cl_2 (1:3), afforded 530 mg of a mixture, which was analyzed on HPLC yielding 400 mg (1.35 mmol, 65%) of **8a** as a liquid: ^{1}H NMR δ 1.58–2.15 (m, 4H, $2CH_2$), 2.88–3.06 (m, 4H, CH_2NCH_2), 3.89 (s, 3H, OMe), 6.86–7.53 (m, 4H, Ar); IR (neat) 2220 (C≡N) cm^{-1}; MS (*m*/*z*) 293 (M$^+$). Anal. Calcd for $C_{13}H_{15}N_3OS_2$: C, 53.22; H, 5.15; N, 14.32; S, 21.85. Found: C, 53.15; H, 5.11; N, 14.30; S, 22.67.

(*p*-Tolylimino)cyanomethyl (Butane-1,4-diyl)amino Disulfide (8b). The reaction of 211 mg (0.869 mmol) of **1b** with 0.15 mL (1.8 mmol) of pyrrolidine in 30 mL of CH_2Cl_2, followed by chromatography using a mixture of petroleum ether and CH_2Cl_2 (1:2), afforded 193 mg of a mixture, which was analyzed on HPLC yielding 16 mg (0.487 mmol, 8%) of **1b** and 135 mg (0.487 mmol, 56%) of **8b** as a liquid: ^{1}H NMR δ 1.60–2.05 (m, 4H, $2CH_2$), 2.43 (s, 3H, Me), 2.90–3.40 (m, 4H, CH_2NCH_2), 6.90–7.54 (m, 4H, Ar); IR (neat) 2210 (C≡N) cm^{-1}; MS (*m*/*z*) 277 (M$^+$). Anal. Calcd for $C_{13}H_{15}N_3S_2$: C, 56.29; H, 5.45; N, 15.15; S, 23.11. Found: C, 56.04; H, 5.32; N, 15.01; S, 23.63. Elution next with CH_2Cl_2 afforded 34 mg (0.160 mmol, 18%) of *N'*-(*p*-tolyl)-*N*,*N*-(butane-1,4-diyl)cyanoformamidine (**12b**) that was recrystallized from *n*-hexane, mp 67–69 °C.

[(*p*-Nitrophenyl)imino]cyanomethyl (Butane-1,4-diyl)amino Disulfide (8c). The reaction of 247 mg (0.902 mmol) of **1c** with 0.17 mL (2.0 mmol) of pyrrolidine in 30 mL of CH_2Cl_2, followed by chromatography using a mixture of petroleum ether and CH_2Cl_2 (1:1) afforded an unknown mixture (20 mg). Elution with the same solvent mixture (2:3) afforded 187 mg of a mixture which was analyzed on HPLC yielding 130 mg (0.423 mmol, 47%) of **8c** as a liquid: ^{1}H NMR δ 1.60–2.26 (m, 4H, $2CH_2$), 2.97–3.50 (m, 4H, CH_2NCH_2), 7.10–7.60 (m, 2H, Ar), 8.59 (d, J = 9 Hz, 2H, Ar); IR (neat) 2220 (C≡N) cm^{-1}; MS (*m*/*z*) 308 (M$^+$). Anal. Calcd for $C_{12}H_{12}N_4O_2S_2$: C, 46.74; H, 3.92; N, 18.17; S, 20.79. Found: C, 46.59; H, 3.85; N, 18.14; S, 21.31. Elution with CH_2Cl_2 afforded 39 mg (0.158 mmol, 18%) of *N'*-(*p*-nitrophenyl)-*N*,*N*-(butane-1,4-diyl)cyanoformamidine (**12c**) as a liquid: ^{1}H NMR δ 1.85–2.35 (m, 4H, $2CH_2$), 3.42–4.17 (m, 4H, CH_2NCH_2), 7.25 (d, J = 9 Hz, 2H, Ar), 8.49 (d, J = 9 Hz, 2H, Ar); IR (neat) 2240 (C≡N) cm^{-1}; MS (*m*/*z*) 244 (M$^+$). Anal. Calcd for $C_{12}H_{12}N_4O_2$: C, 59.01; H, 4.91; N, 22.94. Found: C, 58.99; H, 4.87; N, 22.90.

(*p*-Anisylimino)cyanomethyl Isopropylamino Disulfide (9a). The reaction of 1.00 g (3.86 mmol) of **1a** with 0.66 mL (7.8

mmol) of isopropylamine in 50 mL of CH_2Cl_2, followed by chromatography using a mixture of petroleum ether and CH_2Cl_2 (1:1) afforded 365 mg (1.41 mmol, 37%) of **1a**. Continuous elution with the same solvent mixture (1:1) afforded 381 mg of a mixture, which was analyzed on HPLC yielding 184 mg (0.711 mmol, 18%) of **1a**, and 156 mg (0.556 mmol, 14%) of **9a** as a liquid: ^{1}H NMR δ 1.17 (d, J = 7 Hz, 6H, CMe_2), 2.89–3.45 (m, 1H, CH), 3.55–4.07 (m, 4H, NH, OMe), 6.75–7.46 (m, 4H, Ar); IR (neat) 3310 (N–H), 2218 (C≡N) cm^{-1}; MS (m/z) 281 (M^+). Anal. Calcd for $C_{12}H_{15}N_3OS_2$: C, 51.22; H, 5.37; N, 14.93; S, 22.79. Found: C, 51.19; H, 5.32; N, 14.87; S, 23.60.

(*p*-Tolylimino)cyanomethyl Isopropylamino Disulfide (9b). The reaction of 318 mg (1.31 mmol) of **1b** with 0.25 mL (2.9 mmol) of isopropylamine in 30 mL of CH_2Cl_2, followed by chromatography using a mixture of petroleum ether and CH_2Cl_2 (1:2) afforded 280 mg of a mixture, which was rechromatographed using the same solvent mixture (2:1) to give 156 mg (0.643 mmol, 49%) of **1b**. Continuous elution with the same solvent mixture (1:1) gave 81 mg (0.305 mmol, 23%) of **9b** as a liquid: ^{1}H NMR δ 1.20 (d, J = 7 Hz, 6H, CMe_2), 2.43 (s, 3H, Me), 3.05–4.07 (m, 2H, NH, CH), 6.84–7.56 (m, 4H, Ar); IR (neat) 3325 (N–H), 2220 (C≡N) cm^{-1}; MS (m/z) 265 (M^+). Anal. Calcd for $C_{12}H_{15}N_3S_2$: C, 54.31; H, 5.70; N, 15.83; S, 24.16. Found: C, 54.23; H, 5.59; N, 15.58; S, 24.61.

(*p*-Nitrophenylimino)cyanomethyl Diethylamino Disulfide (10). The reaction of 511 mg (1.87 mmol) of **1c** with 0.25 mL (3.8 mmol) of diethylamine in 30 mL of CH_2Cl_2, followed by chromatography using a mixture of petroleum ether and CH_2Cl_2 (1:3) afforded 254 mg of a mixture which was analyzed on HPLC yielding 210 mg (0.677 mmol, 36%) of **10** as a liquid: ^{1}H NMR (80 MHz) δ 1.22 (t, J = 7 Hz, 6H, 2Me), 3.10 (q, J = 7 Hz, 4H, CH_2NCH_2), 6.90–7.25 (m, 2H, Ar), 8.29 (d, J = 9 Hz, 2H, Ar); IR (neat) 2227 (C≡N) cm^{-1}; MS (m/z) 310 (M^+). Anal. Calcd for $C_{12}H_{14}N_4O_2S_2$: C, 46.44; H, 4.55; N, 18.05; S, 20.66. Found: C, 45.32; H, 4.54; N, 18.01; S, 21.23.

***N'*-(*p*-Tolyl)-*N,N*-(pentane-1,5-diyl)cyanoformamidine (11b).** The reaction of 500 mg (2.06 mmol) of **1b** with 0.60 mL (6.1 mmol) of piperidine in 20 mL of CH_2Cl_2, followed by chromatography using a mixture of petroleum ether and CH_2Cl_2 (3:1) gave 303 mg of complex mixtures. Elution next with CH_2Cl_2 afforded 203 mg (1.00 mmol, 49%) of **11b** as a liquid: ^{1}H NMR δ 1.42–1.95 (m, 6H, $3CH_2$), 2.35 (s, 3H, Me), 3.50–4.00 (m, 4H, CH_2NCH_2), 7.03 (d, J = 8 Hz, 2H, Ar), 7.36 (d, J = 8 Hz, 2H, Ar); IR (neat) 2220 (C≡N) cm^{-1}; MS (m/z) 227 (M^+). Anal. Calcd for $C_{14}H_{17}N_3$: C, 73.98; H, 7.54; N, 18.49. Found: C, 73.91; H, 7.52; N, 18.57. Finally, elution with a mixture of CH_2Cl_2 and ethyl ether (5:1) afforded 45 mg (0.192 mmol, 9%) of *N,N*-(pentane-1,5-diyl)-*N'*-(*p*-tolyl)thiourea (**16**) which was recrystallized from a mixture of petroleum ether and CH_2Cl_2: mp 132–133 °C; ^{1}H NMR (80 MHz) δ 1.45–1.80 (m, 6H, $3CH_2$), 2.31 (s, 3H, Me), 3.60–3.90 (m, 4H, CH_2NCH_2), 6.90–7.25 (m, 5H, Ar, NH); IR (KBr) 3200 (N–H) cm^{-1}; MS (m/z) 220 (M^+). Anal. Calcd for $C_{12}H_{16}N_2S$: C, 65.42; H, 7.32; N, 12.71; S, 14.55. Found: C, 65.35; H, 7.27; N, 12.37; S, 15.01.

***N'*-(*p*-Nitrophenyl)-*N,N*-(pentane-1,5-diyl)cyanoformamidine (11c).** (i) The reaction of 505 mg (1.85 mmol) of **1c** with 0.75 mL (7.6 mmol) of piperidine in 40 mL of CH_2Cl_2, followed by chromatography using a mixture of petroleum ether and CH_2Cl_2 (2:1), gave 200 mg (0.757 mmol, 62%) of bis(piperidino) trisulfide (**23**), which was recrystallized from methanol: mp 74–74.5 °C (lit.[13] mp 74 °C). Elution next with the same solvent mixture (1:1) afforded 225 mg (0.871 mmol, 47%) of **11c**, which was recrystallized from *n*-hexane: mp 113–114 °C; ^{1}H NMR δ 1.50–2.05 (m, 6H, $3CH_2$), 3.55–4.03 (m, 4H, CH_2NCH_2), 7.20 (d, J = 9 Hz, 2H, Ar), 8.43 (d, J = 9 Hz, 2H, Ar); IR (KBr) 2220 (C≡N) cm^{-1}; MS (m/z) 258 (M^+). Anal. Calcd for $C_{13}H_{14}N_4O_2$: C, 60.45; H, 5.46; N, 21.69. Found: C, 60.31; H, 5.48; N, 21.72. (ii) The solution of 581 mg (1.80 mmol) of **7c** and 0.55 mL (5.6 mmol) of piperidine in 30 mL of CH_2Cl_2 was stirred for 12 h at room temperature. Chromatography of the reaction mixture as in the case of i gave 193 mg (0.730 mmol, 61%) of **23** and 201 mg (0.778 mmol, 43%) of **11c**. (iii) The solution of 120 mg (0.372 mmol) of **7c** and 0.40 mL (4.7 mmol) of isopropylamine in 30 mL of CH_2Cl_2 was refluxed for 5 h. Chromatography using a mixture of petroleum ether and CH_2Cl_2 (1:2) gave 42 mg (0.164 mmol, 44%) of **11c**. Elution next with CH_2Cl_2 afforded 39 mg (0.167 mmol, 45%) of *N'*-(*p*-nitrophenyl)-*N*-isopropylcyanoformamidine (**15b**), which was recrystallized from *n*-hexane: mp 87–89 °C; ^{1}H NMR δ 1.30 (d, J = 7 Hz, 6H, CMe_2), 3.93–4.63 (m, 1H, CH), 5.53 (s, 1H, NH), 7.22 (d, J = 9 Hz, 2H, Ar), 8.43 (d, J = 9 Hz, 2H, Ar); IR (KBr) 3350, 3200 (N–H) cm^{-1}; MS (m/z) 232 (M^+). Anal. Calcd for $C_{11}H_{12}N_4O_2$: C, 56.89; H, 5.21; N, 24.12. Found: C, 56.92; H, 5.18; N, 24.15. (iv) The solution of 267 mg (0.828 mmol) of **7c** and 0.80 mL (7.5 mmol) of *tert*-butylamine in 20 mL of CH_2Cl_2 was refluxed for 5 h. Chromatography as in the case of iii afforded 105 mg (0.407 mmol, 49%) of **11c**. (v) The solution of 360 mg (1.12 mmol) of **7c** and 572 mg (12.7 mmol) of ethylamine in 20 mL of CH_2Cl_2 was stirred at room temperature for 15 h. Chromatography of the reaction mixture using a mixture of petroleum ether and CH_2Cl_2 (1:1) gave 76 mg of a mixture. Continuous elution with the same solvent mixture (1:3) afforded 15 mg (0.0581 mmol, 5%) of **11c**. Elution next with a mixture of CH_2Cl_2 and ethyl ether (5:1) afforded 60 mg (0.275 mmol, 25%) of *N'*-(*p*-nitrophenyl)-*N*-ethylcyanoformamidine (**14**), which was recrystallized from a mixture of *n*-hexane and CH_2Cl_2: mp 85–86 °C; ^{1}H NMR (80 MHz) δ 1.30 (t, J = 7 Hz, 3H, Me), 3.51 (q, J = 7 Hz, 2H, NCH_2), 5.29 (s, 1H, NH), 7.05 (d, J = 8 Hz, 2H, Ar), 8.23 (d, J = 8 Hz, 2H, Ar); IR (KBr) 3360, 3300 (N–H) cm^{-1}; MS (m/z) 218 (M^+). Anal. Calcd for $C_{10}H_{10}N_4O_2$: C, 55.04; H, 4.62; N, 25.68. Found: C, 54.98; H, 4.60; N, 25.70. (vi) The solution of 489 mg (1.52 mmol) of **7c** and 0.60 mL (5.8 mmol) of piperidine in 30 mL of CH_2Cl_2 was stirred for 24 h at room temperature. Chromatography of the reaction mixture as in the case of i gave 85 mg (0.329 mmol, 22%) of **11c**.

***N'*-(*m*-Nitrophenyl)-*N,N*-(pentane-1,5-diyl)cyanoformamidine (11d).** (i) The solution of 468 mg (1.71 mmol) of **1d** and 1.0 mL (10 mmol) of piperidine in 30 mL of CH_2Cl_2 was stirred for 30 h at room temperature. Chromatography using a mixture of petroleum ether and CH_2Cl_2 (5:2) afforded 115 mg (0.491 mmol, 43%) of **23**. Elution next with the same solvent mixture (2:3) afforded 77 mg of a mixture. Continuous elution with the same solvent mixture (1:3) afforded 116 mg (0.448 mmol, 26%) of **11d**, which was recrystallized from *n*-hexane: mp 83–84 °C; ^{1}H NMR (80 MHz) 1.60–1.90 (m, 6H, $3CH_2$), 3.50–3.80 (m, 4H, CH_2NCH_2), 7.13–8.07 (m, 4H, Ar); IR (neat) 2220 (C≡N) cm^{-1}; MS (m/z) 258 (M^+). Anal. Calcd for $C_{13}H_{14}N_4O_2$: C, 60.45; H, 5.46; N, 21.69. Found: C, 60.57; H, 5.44; N, 21.65. (ii) The solution of 595 mg (2.19 mmol) of **1d** and 0.86 mL (8.7 mmol) of piperidine in 40 mL of CH_2Cl_2 was stirred for 4 h at room temperature. Chromatography of the mixture as in the case of i gave 88 mg (0.331 mmol, 23%) of **23** and 81 mg (0.312 mmol, 14%) of **11d**. (iii) The solution of 193 mg (0.599 mmol) of **7d** and 0.3 mL (3.0 mmol) of piperidine in 20 mL of CH_2Cl_2 was stirred for 30 h at room temperature. Chromatography of the mixture as in the case of i gave 39 mg (0.158 mmol, 26%) of **23** and 34 mg (0.132 mmol, 22%) of **11d**.

***N'*-(*p*-Anisyl)-*N,N*-(butane-1,4-diyl)cyanoformamidine (12a).** (i) The solution of 323 mg (1.25 mmol) of **1a** and 0.4 mL (4.8 mmol) of pyrrolidine in 20 mL of CH_2Cl_2 was stirred for 1 h at room temperature. Chromatography using a mixture of petroleum ether and CH_2Cl_2 (3:1) afforded 76 mg of an unknown mixture. Continuous elution with the same solvent mixture (1:3) afforded 253 mg (1.10 mmol, 88%) of **12a** as a liquid: ^{1}H NMR δ 1.35–1.56 (m, 4H, $2CH_2$), 3.35–3.94 (m, 7H, OMe, CH_2NCH_2), 6.93 (s, 4H, Ar); IR (neat) 2230 (C≡N) cm^{-1}; MS (m/z) 229 (M^+). Anal. Calcd for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59; N, 18.33. Found: C, 68.13; H, 6.57; N, 18.29. (ii) The solution of 50 mg (0.163 mmol) of **7a** and 0.10 mL (1.2 mmol) of pyrrolidine in 10 mL of CH_2Cl_2 was stirred for 1.5 h at room temperature. Chromatography of the reaction mixture using CH_2Cl_2 gave 36 mg (0.158 mmol, 97%) of **12a**. (iii) The solution of 120 mg (0.624 mmol) of *N*-(*p*-anisyl)cyanothioformamide (**19a**) and 0.25 mL (3.0 mmol) of pyrrolidine in 20 mL of CH_2Cl_2 was stirred for 10 min at room temperature. Chromatography, as in the case of ii, afforded 95 mg (0.414 mmol, 66%) of **12a**.

***N'*-(*p*-Tolyl)-*N,N*-(butane-1.4-diyl)cyanoformamidine (12b).** The solution of 502 mg (2.07 mmol) of **1b** and 0.50 mL (6.0 mmol) of pyrrolidine in 20 mL of CH_2Cl_2 was stirred for 30 min at room temperature. Chromatography using a mixture of petroleum ether and CH_2Cl_2 (2:1) afforded 162 mg of an unknown mixture. Continuous elution with CH_2Cl_2 afforded 263 mg (1.23 mmol, 59%) of **12b**, which was recrystallized from *n*-hexane: mp 67–69 °C; ^{1}H NMR δ 1.80–2.13 (m, 4H, $2CH_2$), 2.25 (s, 3H, Me),

3.30–3.77 (m, 4H, CH_2NCH_2), 6.70 (d, J = 8 Hz, 2H, Ar), 6.99 (d, J = 9 Hz, 2H, Ar); IR (KBr) 2222 (C≡N) cm^{-1}; MS (m/z) 213 (M^+). Anal. Calcd for $C_{13}H_{15}N_3$: C, 73.21; H, 7.09; N, 19.70. Found: C, 73.23; H, 7.12; N, 19.65. Elution next with a mixture of ethyl ether and CH_2Cl_2 (1:5) gave 109 mg (0.511 mmol, 25%) of **12b**. Continuous elution with a mixture of ethyl ether and CH_2Cl_2 (1:5) gave 53 mg (0.24 mmol, 12%) of *N,N*-(butane-1,4-diyl)-*N'*-(*p*-tolyl)thiourea (**17a**) which was recrystallized from a mixture of petroleum ether and CH_2Cl_2: mp 164–166 °C; ^1H NMR (80 MHz) δ 1.97–2.13 (m, 4H, $2CH_2$), 2.33 (s, 3H, Me), 3.46–3.80 (m, 4H, CH_2NCH_2), 6.89 (s, 1H, NH), 7.04–7.30 (m, 4H, Ar); IR (KBr) 3334 (N–H) cm^{-1}; MS (m/z) 220 (M^+). Anal. Calcd for $C_{12}H_{16}N_2S$: C, 65.42; H, 7.32; N, 12.71; S, 14.55. Found: C, 65.22; H, 7.31; N, 12.55; S, 14.92.

***N'*-(*p*-Nitrophenyl)-*N,N*-(butane-1,4-diyl)cyanoformamidine (12c).** (i) The solution of 265 mg (0.822 mmol) of **7c** and 0.50 mL (6.0 mmol) of pyrrolidine in 30 mL of CH_2Cl_2 was stirred for 1.5 h at room temperature. Chromatography using CH_2Cl_2 afforded 67 mg of a mixture, which was rechromatography to give 48 mg (0.198 mmol, 24%) of **12c**. Continuous elution of the original reaction mixture with a mixture of CH_2Cl_2 and ethyl ether (5:1) gave 100 mg (0.398 mmol, 48%) of *N,N*-(butane-1,4-diyl)-*N'*-(*p*-nitrophenyl)thiourea (**17b**) which was recrystallized from a mixture of *n*-hexane and CH_2Cl_2: mp 204–208 °C; ^1H NMR ($CDCl_3$ + DMSO-d_6, 80 MHz) δ 1.90–2.20 (m, 4H, $2CH_2$), 3.60–3.90 (m, 4H, CH_2NCH_2), 7.75 (d, J = 9 Hz, 2H, Ar), 8.14 (d, J = 9 Hz, 2H, Ar), 9.02 (s, 1H, NH); IR (KBr) 3232 (N–H) cm^{-1}. (ii) The solution of 181 mg (0.874 mmol) of *N*-(*p*-nitrophenyl)-cyanothioformamide (**19c**) and 0.35 mL (4.2 mmol) of pyrrolidine in 20 mL of CH_2Cl_2 was stirred for 10 min at room temperature. Chromatography using CH_2Cl_2 afforded 29 mg (0.119 mmol, 14%) of **12c**. Continuous elution with ethyl ether afforded 85 mg (0.338 mmol, 39%) of **17b**.

***N'*-(*p*-Anisyl)-*N,N*-(3-oxapentane-1,5-diyl)cyanoformamidine (13a).** (i) The solution of 265 mg (1.02 mmol) of **1a** and 0.40 mL (4.6 mmol) of morpholine in 30 mL of CH_2Cl_2 was stirred for 1 h at room temperature. Chromatography using a mixture of petroleum ether and CH_2Cl_2 (1:1), followed by CH_2Cl_2, gave 217 mg (0.884 mmol, 87%) of **13a** which was recrystallized from *n*-hexane: mp 73–74 °C; ^1H NMR δ 3.50–4.00 (m, 11H, $4CH_2$, OMe), 6.95 (s, 4H, Ar); IR (KBr) 2220 (C≡N) cm^{-1}; MS (m/z) 245 (M^+). Anal. Calcd for $C_{13}H_{15}N_3O_2$: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.52; H, 6.18; N, 17.20. (ii) The solution of 509 mg (1.97 mmol) of **1a** and 0.35 mL (4.0 mmol) of morpholine in 30 mL of CH_2Cl_2 was stirred for 1.5 h. Chromatography using a mixture of petroleum ether and CH_2Cl_2 (1:1) gave 253 mg (0.978 mmol, 50%) of **1a**. Continuous elution with a mixture of CH_2Cl_2 and ethyl ether (5:1) gave 109 mg (0.444 mmol, 23%) of **13a**.

***N'*-(*p*-Tolyl)-*N,N*-(3-oxapentane-1,5-diyl)cyanoformamidine (13b).** The solution of 560 mg (2.31 mmol) of **1b** and 0.59 mL (6.8 mmol) of morpholine in 30 mL of CH_2Cl_2 was stirred for 2.5 h at room temperature. Chromatography using a mixture of CH_2Cl_2 and ethyl ether (9:1) afforded 492 mg of a mixture, which was analyzed on HPLC yielding 406 mg (1.77 mmol, 77%) of **13b**, which was recrystallized from *n*-hexane: mp 76–77 °C; ^1H NMR δ 2.41 (s, 3H, Me), 3.60–4.05 (m, 8H, $4CH_2$), 6.99 (d, J = 8 Hz, 2H, Ar), 7.33 (d, J = 8 Hz, 2H, Ar); IR (neat) 2223 (C≡N) cm^{-1}; MS (m/z) 229 (M^+). Anal. Calcd for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59; N, 18.33. Found: C, 67.99; H, 6.48; N, 18.83.

***N'*-(*m*-Nitrophenyl)-*N,N*-(3-oxapentane-1,5-diyl)cyanoformamidine (13c).** The solution of 470 mg (1.46 mmol) of **7d** and 0.70 mL (8.1 mmol) of morpholine in 30 mL of CH_2Cl_2 was stirred for 30 min at room temperature. Chromatography using CH_2Cl_2 gave 295 mg (1.13 mmol, 77%) of **13c**, which was recrystallized from a mixture of *n*-hexane and $CHCl_3$: mp 143–144 °C; ^1H NMR (80 MHz) δ 3.60–3.95 (m, 8H, $4CH_2$), 7.14–8.10 (m, 4H, Ar); IR (KBr) 2222 (C≡N) cm^{-1}; MS (m/z) 260 (M^+). Anal. Calcd for $C_{12}H_{12}N_4O_3$: C, 55.38; H, 4.65; N, 21.53. Found: C, 55.41; H, 4.60; N, 21.49.

***N'*-(*p*-Nitrophenyl)-*N*-ethylcyanoformamidine (14).** The solution of 564 mg (2.02 mmol) of **1c** and 715 mg (15.9 mmol) of ethylamine in 30 mL of CH_2Cl_2 was stirred for 15 h at room temperature. Chromatography using a mixture of petroleum ether and CH_2Cl_2 (1:4), followed by CH_2Cl_2, gave 210 mg (0.962 mmol, 48%) of **14** which was recrystallized from *n*-hexane and CH_2Cl_2, mp 85–86 °C.

***N'*-(*p*-Anisyl)-*N*-isopropylcyanoformamidine (15a).** (i) The solution of 191 mg (0.621 mmol) of **7a** and 0.40 mL (4.7 mmol) of isopropylamine in 30 mL of CH_2Cl_2 was refluxed for 3 h. Chromatography using a mixture of petroleum ether and CH_2Cl_2 (1:2), followed by CH_2Cl_2, afforded 40 mg (0.162 mmol, 26%) of **11a**. Elution next with a mixture of CH_2Cl_2 and ethyl ether (10:1) gave 59 mg of a mixture of **15a** and unknown compounds of which separation by HPLC was unsuccessful. (ii) Dry hydrogen chloride gas was bubbled into a soluiotn of 156 mg (0.556 mmol) of **9a** in 30 mL of CH_2Cl_2 for 30 min, which was worked up as usual. Chromatography of the reaction mixture using a mixture of petroleum ether and CH_2Cl_2 (2:1) gave 56 mg (0.295 mmol, 51%) of *N*-(*p*-anisyl)cyanoimidoyl chloride (**18**) which was recrystallized from *n*-hexane: mp 28–28.5 °C; ^1H NMR δ 3.90 (s, 3H, OMe), 7.00 (d, J = 9 Hz, 2H, Ar), 7.50 (d, J = 9 Hz, 2H, Ar); IR (neat) 2228 (C≡N), 1640 (C=N) cm^{-1}; MS (m/z) 194 (M^+). Anal. Calcd for $C_9H_7ClN_2O$: C, 55.54; H, 3.63; N, 14.39. Found: C, 55.42; H, 3.65; N, 14.46. To a solution of 130 mg (0.666 mmol) of 18 in 10 mL of CH_2Cl_2 was added 0.2 mL (2.3 mmol) of isopropylamine. Workup of the reaction mixture gave 141 mg (0.649 mmol, 97%) of **15a** which was recrystallized from *n*-hexane and CH_2Cl_2: mp 110–112 °C; ^1H NMR δ 1.25 (d, J = 7Hz, 6H, CMe_2), 3.89 (s, 3H, OMe), 3.89–4.63 (m, 1H, CH), 4.88 (s, 1H, NH), 7.07 (s, 4H, Ar); IR (KBr) 3245 (N–H), 2229 (C≡N) cm^{-1}; MS (m/z) 217 (M^+). Anal. Calcd for $C_{12}H_{15}N_3O$: C, 66.34; H, 6.96; N, 19.34. Found: C, 66.37; H, 6.92; N, 19.33.

***N,N*-(Butane-1,4-diyl)-*N'*-(*o*-carbethoxyphenyl)thiourea (17c).** A mixture of 202 mg (0.862 mmol) of **19e** and 0.40 mL (4.8 mmol) of pyrrolidine in 20 mL of CH_2Cl_2 was stirred for 5 min at room temperature. Chromatography of the reaction mixture using a mixture of petroleum ether and CH_2Cl_2 (1:2) afforded 229 mg (0.823 mmol, 95%) of **17c**, which was recrystallized from *n*-hexane and CH_2Cl_2: mp 137–139 °C; ^1H NMR (80 MHz) δ 1.40 (t, J = 7 Hz, 3H, Me), 1.80–2.30 (m, 4H, $2CH_2$), 3.60–4.10 (m, 4H, CH_2NCH_2), 4.36 (q, J = 7 Hz, 2H, OCH_2), 6.90–8.10 (m, 3H, Ar), 9.04 (dd, J = 9, 1 Hz, 1H, Ar), 10.89 (1H, s, NH); IR (KBr) 3240 (N–H) cm^{-1}; MS (m/z) 278 (M^+). Anal. Calcd for $C_{14}H_{18}N_2O_2S$: C, 60.40; H, 6.52; N, 10.06; S, 11.52. Found: C, 60.35; H, 6.50; N, 10.02; S, 12.01.

***N*-(Arylimino)cyanothioformamides (19).** Cyanothioformamides **19** were prepared by the literature method.[16]

***N*-(*p*-Anisyl)cyanothioformamide (19a):** mp 121–122 °C (lit.[17] mp 118–120 °C).

***N*-(*p*-Tolyl)cyanothioformamide (19b):** mp 130–131 °C (lit.[17] mp 126.5–128.5 °C).

***N*-(*p*-Nitrophenyl)cyanothioformamide (19c):** mp 128–130 °C (lit.[10d] mp 128–130 °C).

***N*-(*m*-Nitrophenyl)cyanothioformamide (19d):** mp 103–104 °C (lit.[17] mp 99–102 °C).

***N*-(*o*-Carbethoxyphenyl)cyanothioformamide (19e):** mp 89–90 °C; ^1H NMR δ 1.45 (t, J = 7 Hz, 3H, Me), 4.47 (q, J = 7 Hz, 2H, OCH_2), 7.35 (dt, J = 1, 8 Hz, 1H, Ar), 7.64 (dt, J = 2, 8 Hz, 1H, Ar), 8.18 (dd, J = 2, 8 Hz, 1H, Ar), 9.35 (d, J = 8 Hz, 1H, Ar), 13.42 (s, 1H, NH); IR (KBr) 2225 (C≡N), 1678 (C=O) cm^{-1}; MS (m/z) 234 (M^+). Anal. Calcd for $C_{11}H_{10}N_2O_2S$: C, 56.40; H, 4.30; N, 11.96; S, 13.68. Found: C, 56.25; H, 4.21; N, 11.95; S, 14.42.

Reactions of 1c with Isopropylamine. A mixture of 296 mg (1.08 mmol) of **1c** and 0.20 mL (2.3 mmol) of isopropylamine in 50 mL of CH_2Cl_2 was stirred for 1.5 h at room temperature. Chromatography of the reaction mixture using a mixture of petroleum ether and CH_2Cl_2 (1:2) gave 160 mg of a mixture of **1c** from which 140 mg (0.511 mmol, 47%) of **1c** was recovered by recrystallization from a mixture of *n*-hexane and CH_2Cl_2.

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