Novel Synthesis of 5-(Arylimino)-4-(dialkylamino)-5*H*-1,2,3-dithiazoles and the Mechanism of Their Formation§

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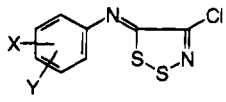
The reactions of 5-(arylimino)-4-chloro-5*H*-1,2,3-dithiazoles **1** with excess (6 equiv) bulky dialkylamines such as diethyl-, di-*n*-propyl-, and di-*n*-butylamines in CH_2Cl_2 at room temperature gave 5-(arylimino)-4-(dialkylamino)-5*H*-1,2,3-dithiazoles **5** in 18–76% yields. Compounds **5** are formed via (arylimino)cyanomethyl alkylamino disulfides **3**. Nucleophilic addition of the amines to the carbon atom of the cyano group of **3** and subsequent cyclization afford **5**.

Since a synthesis of 5-(arylimino)-4-chloro-5*H*-1,2,3-dithiazoles **1** was reported,[1] much attention has been focused on these compounds because of their potential synthetic utility[2] and biological importance.[1,3] Compounds **1** are heteroaromatic compounds having nucleophilic centers at the S1, S2, C4, and C5 positions. Several reactions involving either C5 or S1 as a nucleophilic center have been reported.[3b] The formation of dithiazolobenzoxazine **2** from the reaction of 4-chloro-5-[(*o*-hydroxyphenyl)imino]-5*H*-1,2,3-dithiazole (**1**) (X = 2-OH, Y = H) with NaH in THF, reported by Rees *et al.*,[3b] was the first example of the intramolecular nucleophilic displacement of the chlorine atom at C4 by phenoxide ion. Interestingly, the intermolecular equivalent of this



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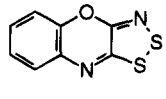

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cyclization was reported to be unsuccessful with sodium phenoxide and 4-chloro-5-(phenylimino)-5*H*-1,2,3-dithiazole (**1**) (X = Y = H) even under more vigorous conditions.[3b] Recently[4] we have demonstrated the involvement of S2 as a nucleophilic center by isolation of a variety of (arylimino)cyanomethyl (alkyl)amino disulfides **3** from the reactions of **1** with either primary or secondary alkylamines as shown in Scheme 1.

Further reactions of compounds **3** with alkylamines afforded either the corresponding cyanoformamidines **4** or complex mixtures, depending on the amines used and on the substituents on the *N*-phenyl group. When [(*p*-nitrophenyl)imino]cyanomethyl (pentane-1,5-diylamino disulfide **3** (X = *p*-NO_2, Y = H, $R_2 = -CH_2(CH_2)_3CH_2-$) was treated with a sterically bulky amine such as *tert*-butylamine (9 equiv) at reflux or diethylamine (4 equiv) at room temperature, cyanoformamidine **4** (X = *p*-NO_2, Y = H, $R_2 = -CH_2(CH_2)_3CH_2-$) was isolated in 49 or 22% yield, respectively, instead of the cyanoformamidine having either a *tert*-butyl- or a diethylamino group, regardless of the reaction time. From the reaction with isopropylamine (12 equiv) were isolated two different cyanoformamidines **4** (X = *p*-NO_2, Y = H, R_2 = *i*-Pr and X = *p*-NO_2, Y = H, $R_2 = -CH_2(CH_2)_3CH_2-$) in 45 and 44% yields, respectively. However, the reaction of **3** (X = *p*-MeO, Y = H, $R_2 = -CH_2(CH_2)_3CH_2-$) with isopropylamine (8 equiv) gave only complex mixtures and cyanoformamidine **4** (X = *p*-MeO, Y = H, $R_2 = -CH_2(CH_2)_3CH_2-$) in 26% yield.[4]

As part of a mechanistic study of the reactions, we needed to explore the scope of the reactions of **1** with various bulky alkylamines. Herein we wish to report the results.

Results and Discussion

The reactions of compounds **1** (1–2 mmol) with excess amounts (6 equiv) of bulky secondary alkylamines in methylene chloride (30 mL) at room temperature gave 5-(arylimino)-4-(dialkylamino)-5*H*-1,2,3-dithiazoles **5**. The results are summarized in Table 1. The structures of **5** were determined on the basis of spectroscopic and mass spectral data and microanalyses. X-ray single crystallographic analysis[5] of **5d** shows clearly the bonding position of the diethylamino group. Compounds **5** are the result of intramolecular displacement of the C4 chlorine atom of compounds **1** by nucleophiles. In order to determine whether disulfides **3** act as intermediates for the formation of compounds **5**, disulfide **3d** (X = 5-NO_2, Y = 2-Cl, R = Et) was treated with diethylamine (8 equiv) in methylene chloride at room temperature for 6 h to give **5d** in 26% yield. This result indicates that compounds **5** can indeed be formed via the intermediacy of disulfides **3**. The reactions were monitored by the absorption spectroscopic method. From a stirred solution of **1f** (X = 3-NO_2, Y = 4-Cl, 321 mg, 1.04 mmol) and di-*n*-propylamine (0.90 mL, 6.6 mmol) in methylene chloride (25 mL, total volume) at room temperature, a 60 μL aliquot of the reaction mixture was removed and diluted to 25 mL with methylene chloride (1.0×10^{-4} M based on **1f**). The absorption spectra of the solution were

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(1) Appel, R.; Janssen, H.; Siray, M.; Knoch, F. *Chem. Ber.* **1985**, *118*, 1632.
(2) (a) Moore, J. E. U.S. Patent 4059590, 1977; *Chem. Abstr.* **1978**, *88*, 50874a. (b) Mayer, R.; Foerster, E.; Matauschek, B. Ger (East) DD. 212387, 1984; *Chem. Abstr.* **1985**, *102*, 113064s.
(3) (a) Oh, K. C.; Lee, H.; Kim, K. *Tetrahedron Lett.* **1992**, *33*, 4963. (b) Rees, C. W. *J. Heterocycl. Chem.* **1992**, *29*, 639. (c) Folmer, J. J.; Weinreb, S. M. *Tetrahedron Lett.* **1993**, *34*, 2737.
(4) Lee, H.; Kim, K. *J. Org. Chem.* **1993**, *58*, 7001.
(5) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

0022-3263/94/1959-6179$04.50/0

Scheme 1

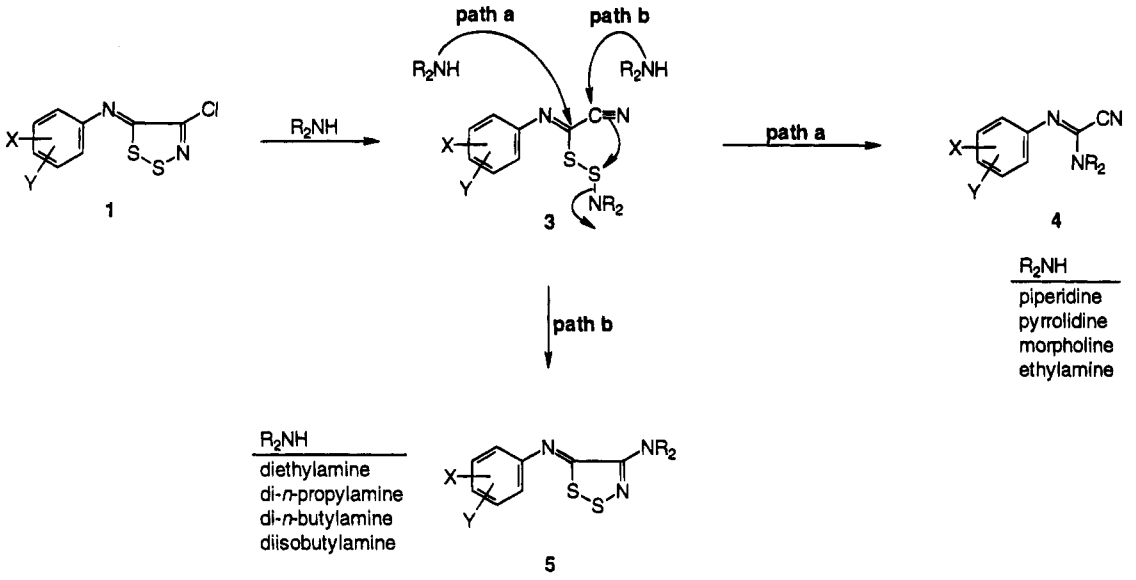


Table 1. Preparation of 5-(Arylimino)-4-(dialkylamino)-5*H*-1,2,3-dithiazoles 5

entry	1 (X,Y)	R	reaction time (h)	yield[a] (%)
1	**a** (3-NO_2, H)	Et	48	**5a**, (37)
2	**b** (4-NO_2, H)	Et	48	**5b**, (26)
3	**c** (3-NO_2, 4-Cl)	Et	24	**5c**, (38)
4	**d** (5-NO_2, 2-Cl)	Et	6	**5d**, (32)
5	**a** (3-NO_2, H)	*n*-Pr	48	**5e**, (47)
6	**c** (3-NO_2, 4-Cl)	*n*-Pr	48	**5f**, (75)
7	**b** (4-NO_2, H)	*n*-Pr	48	**5g**, (60)
8	**d** (5-NO_2, 2-Cl)	*n*-Pr	48	**5h**, (76)
9	**e** (4-Br, H)	*n*-Pr	48	**5i**, (59)
10	**f** (4-MeO, H)	*n*-Pr	48	**5j**, (23)
11	**g** (4-Me, H)	*n*-Pr	48	**5k**, (18)
12	**b** (4-NO_2, H)	allyl	48	**5l**, (20)
13	**c** (3-NO_2, 4-Cl)	*n*-Bu	24	**5m**, (63)
14	**b** (4-NO_2, H)	*n*-Bu	24	**5n**, (63)
15	**e** (4-Br, H)	*n*-Bu	48	**5o**, (59)
16	**b** (4-NO_2, H)	*i*-Bu	72	**5p**, (7)
17	**g** (4-Me, H)	$-CH_2(CH_2)_3CH_2-$	1	**5q**, (14)[b]
18	**g** (4-Me, H)	$-CMeH(CH_2)_3CH_2-$	48	**5r**, (15)

[a] Isolated yields by either chromatography or HPLC. [b] Cyanoformamidine **4** (X = 4-Me, Y = H, R_2 = $-CH_2(CH_2)_3CH_2-$) and *N*-(*p*-tolyl)-*N'*-(pentane-1,5-diyl)thiourea were isolated in 50 and 10% yields, respectively.[4]

sequentially recorded at 292, 310, 376, and 403 nm for 89.3 h. Figure 2 shows the spectra of the reaction mixture after 2 min, 4.2 h, and 89.3 h; and Figure 3 exhibits the absorption spectra of **1f**, **3f** (X = 3-NO_2, Y = 4-Cl, R = *n*-Pr), and **5f** in methylene chloride. By comparing Figure 2 and Figure 3, one can recognize the rapid transformation of **1f** to disulfide **3f**, followed by a slow conversion of **3f** to **5f**. Therefore, a ring-opening and subsequent recyclization is proposed for the mechanism of formation of **5** from **1**, as shown in Scheme 1.

Reaction of **1** with primary alkylamines did not give compounds **5**, regardless of the concentrations of the amines. The same reactions of **1** with secondary alkylamines are greatly affected by substituents on the *N*-phenyl group and by the structures of the amines. An electron-donating substituent on the *N*-phenyl group decreases the yield of **5** (entries 10, 11). Reactions with di-*n*-propyl- (entries 5–8) and di-*n*-butylamines (entries 13, 14) afforded better yields of **5** than reactions with diethylamine (entries 1–4). However, it appears that diisobutylamine is simply too bulky for the reaction

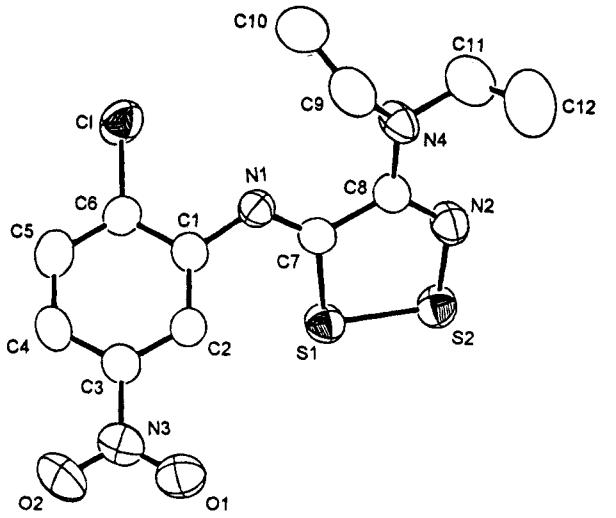
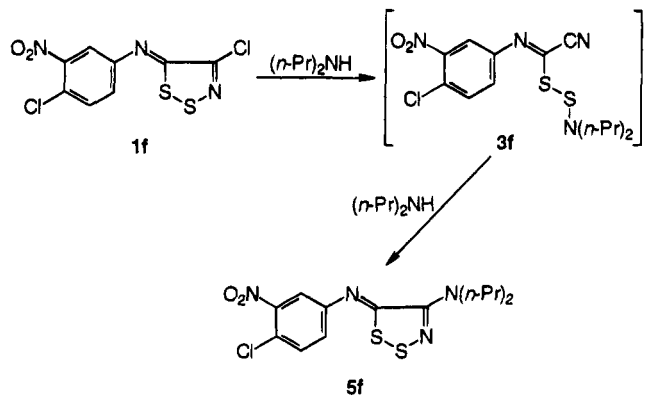


Figure 1. ORTEP drawing of **5d**. Selected bond lengths (Å): S1–S2 2.058 (2), S1–C7 1.760 (6), S2–N2 1.647 (6), N1–C7 1.269 (8), N2–C8 1.302 (8), N4–C8 1.364 (8), C7–C8 1.500 (8). Selected bond angles (deg): S2–S1–C7 94.2 (2), S1–S2–N2 97.8 (2), S2–N2–C8 118.0 (4), C8–N4–C9 125.1 (5), C8–N4–C11 117.5 (6), S1–C7–N1 126.2 (4), S1–C7–C8 110.0 (4), N1–C7–C8 122.7 (5), N2–C8–N4 119.1 (5), N2–C8–C7 119.0 (5), N4–C8–C7 121.7 (5).

(entry 16). The reaction of **1b** with diallylamine (entry 12) afforded a lower yield of the product (**5l**) than did the reaction of **1b** with di-*n*-propylamine (product **5g**, entry 7), in spite of the fact that the alkylamines have the same number of carbon atoms. The reason for the decreased yield of **5l** is not certain. In the case of cyclic amines, the reaction of **1** (X = 4-Me, Y = H) with piperidine gave **5q** in 14% yield (entry 17), and the same reaction with 2-methylpiperidine gave **5r** in 15% yield (entry 18).

In conclusion, both the steric bulkiness of the alkyl groups of the amines and the electronic effects exerted by the substituents on the *N*-phenyl group are important in controlling the regioselectivity of the nucleophilic attack of alkylamines at S2 of **1**. Compounds **5** are formed not by direct displacement of the chlorine atom at C4 but by addition of the amine at the carbon atom of the cyano group of **3** and subsequent cyclization. The



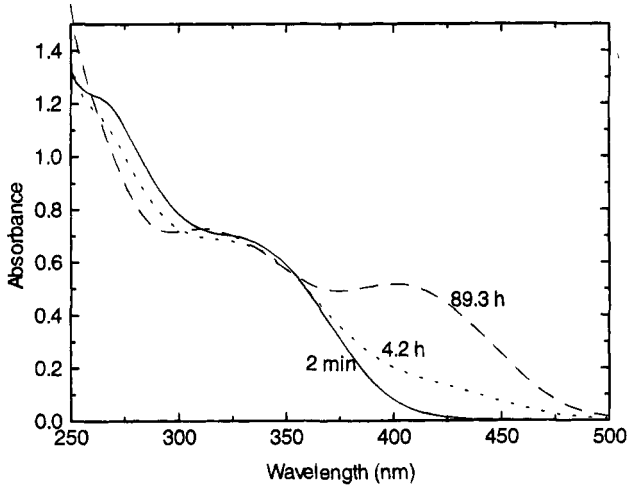


Figure 2. Absorption spectra of a reaction mixture obtained from the reaction of **1f** with *n*-Pr_2NH in CH_2Cl_2 at 2 min, 4.2 h, and 89.3 h.

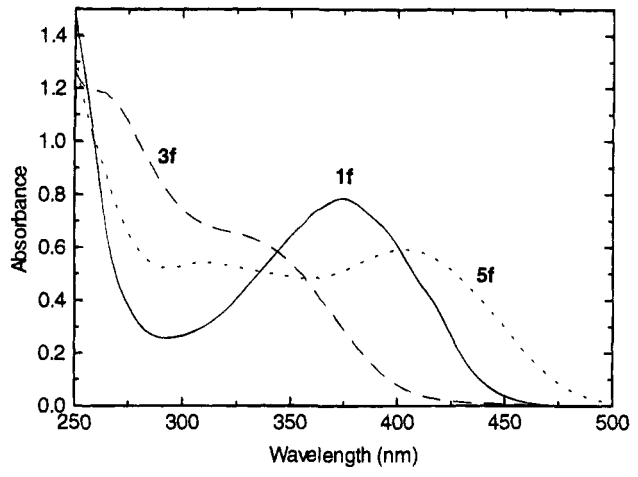


Figure 3. Absorption spectra of **1f**, **3f**, and **5f** in CH_2Cl_2. **1f**: λ_{max} 376 (ϵ 7850) nm; **3f**: λ_{max} 326 (ϵ 6500) nm; **5f**: λ_{max} 403 (ϵ 5930) nm.

scope of the ring-opening of **1**, the subsequent recyclization of **3**, and the dependence of these reactions of the nature of the nucleophiles warrant further study, which is in progress.

Experimental Section

The ^1H NMR spectra were recorded at 80 MHz in $CDCl_3$ solution containing Me_4Si as an internal standard. IR spectra were recorded in KBr or thin films on KBr plates. HPLC was performed with a C-18 column (μBondapak C18, 10 μm, 7.8 × 300 mm i.d.) and a differential refractometer, using CH_3CN as eluant (flow rate = 0.8 mL/min). Elemental analyses were determined by the Korea Basic Science Center. Column chromatography was performed using silica gel (230–400 mesh, Merck). Melting points are uncorrected.

5-(Arylimino)-4-chloro-5*H*-1,2,3-dithiazoles **1** were prepared according to the literature procedures.[1,4]

4-Chloro-5-[(4-chloro-3-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (1c): mp 117–118 °C (EtOH); ^1H NMR δ 7.36 (dd, J = 9, 2 Hz, 1H), 7.64 (d, J = 9 Hz, 1H), 7.76 (d, J = 2 Hz, 1H); IR (KBr) 1570, 1515, 1330 cm^{-1}; MS (*m/z*) 308 (M^+). Anal. Calcd for $C_8H_3Cl_2N_3O_2S_2$: C, 35.18; H, 0.98; N, 13.64; S, 20.81. Found: C, 35.14; H, 1.00; N, 13.45; S, 21.05.

4-Chloro-5-[(2-chloro-5-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (1d): mp 169–171 °C (EtOH); ^1H NMR δ 7.65 (d, J = 9 Hz, 1H), 7.90–8.20 (m, 2H); IR (KBr) 1588, 1510, 1348 cm^{-1}; MS (*m/z*) 308 (M^+). Anal. Calcd for $C_8H_3Cl_2N_3O_2S_2$: C, 35.18; H, 0.98; N, 13.64; S, 20.81. Found: C, 35.16, H, 1.01; N, 13.48; S, 21.10.

5-[(4-Bromophenyl)imino]-4-chloro-5*H*-1,2,3-dithiazole (1e): mp 120–121 °C (EtOH); ^1H NMR δ 7.13 (d, J = 9 Hz, 2H), 7.63 (d, J = 9 Hz, 2H); IR (KBr) 1594, 1482, 1138, 864 cm^{-1}; MS (*m/z*) 308 (M^+ + 2), 306 (M^+). Anal. Calcd for $C_8H_4BrClN_2S_2$: C, 31.24; H, 1.31; N, 9.11; S, 20.84. Found: C, 31.09; H, 1.29; N, 9.14; S, 21.35.

General Procedure for the Reactions of 1 with Dialkylamines. To a solution of **1** (1–2 mmol) in CH_2Cl_2 (30 mL) were added 6 equiv of dialkylamine, and the mixture was stirred for an appropriate time at rt (refer to Table 1). After removal of the solvent in vacuo, the residue was chromatographed on silica gel (1.0 × 15 cm, 230–400 mesh). The bp of petroleum ether used for chromatography was 30–70 °C.

4-(Diethylamino)-5-[(3-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (5a). The reaction of 567 mg (2.07 mmol) of 4-chloro-5-[(3-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (**1a**) with 1.4 mL (14 mmol) of diethylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (3:2), gave 17 mg of an unknown mixture. Continued elution with the same solvent mixture (2:3) afforded 239 mg (37%) of **5a**: yellowish red oil; ^1H NMR δ 1.24 (t, J = 7 Hz, 6H), 3.70 (q, J = 7 Hz, 4H), 7.35–7.70 (m, 2H), 7.93–8.13 (m, 2H); IR (neat) 2990, 1590, 1528, 1350 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, 46.72; H, 4.60; N, 18.21; S, 21.75.

4-(Diethylamino)-5-[(4-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (5b). The reaction of 505 mg (1.85 mmol) of 4-chloro-5-[(4-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (**1b**) with 0.60 mL (9.2 mmol) of diethylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (2:1), gave 52 mg of an unknown mixture. Continued elution with the same solvent mixture (3:2) gave 150 mg (32%) of **5b**, which was recrystallized from *n*-hexane: mp 101–102 °C; ^1H NMR δ 1.24 (t, J = 7 Hz, 6H), 3.69 (q, J = 7 Hz, 4H), 7.33 (d, J = 9 Hz, 2H), 8.31 (d, J = 9 Hz, 2H); IR (KBr) 1592, 1570, 1510, 1334 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, 46.62; H, 4.62; N, 18.17; S, 20.89.

5-[(4-Chloro-3-nitrophenyl)imino]-4-(diethylamino)-5*H*-1,2,3-dithiazole (5c). The reaction of 547 mg (1.76 mmol) of 4-chloro-5-[(4-chloro-3-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (**1c**) with 1.3 mL (13 mmol) of diethylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (10:1), gave 38 mg of an unknown mixture. Elution with the same solvent mixture (4:1) gave 242 mg (38%) of **5c**: yellowish red oil; ^1H NMR δ 1.23 (t, J = 7 Hz, 6H), 3.67 (q, J = 7 Hz, 4H), 7.26 (dd, J = 9, 2 Hz, 1H), 7.58 (d, J = 9 Hz, 1H), 7.63 (d, J = 2 Hz, 1H); IR (neat) 2990, 2950, 1580, 1530, 1350 cm^{-1}; MS (*m/z*) 344 (M^+). Anal. Calcd for $C_{12}H_{13}ClN_4O_2S_2$: C, 41.80; H, 3.80; N, 16.25; S, 18.59. Found: C, 41.75; H, 3.84; N, 16.42; S, 18.88.

5-[(2-Chloro-5-nitrophenyl)imino]-4-(diethylamino)-5*H*-1,2,3-dithiazole (5d). (a) The reaction of 486 mg (1.58 mmol) of 4-chloro-5-[(2-chloro-5-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (**1d**) with 1.1 mL (11 mmol) of diethylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (3:2), gave 10 mg of an unknown

mixture. Elution with the same solvent mixture (2:3) afforded 171 mg (32%) of **5d**, which was recrystallized from *n*-hexane: mp 88–89 °C; ^{1}H NMR δ 1.25 (t, J = 7 Hz, 6H), 3.73 (q, J = 7 Hz, 4H), 7.55–8.06 (m, 3H); IR (neat) 2970, 1570, 1515, 1342 cm^{-1}; MS (*m/z*) 344 (M$^+$). Anal. Calcd for $C_{12}H_{13}N_4ClO_2S_2$: C, 41.80; H, 3.80; N, 16.25; S, 18.59. Found: C, 42.00; H, 3.82; N, 16.26; S, 18.99. (b) The reaction of 129 mg (0.374 mmol) of [(2-chloro-5-nitrophenyl)imino]cyanomethyl diethylamino disulfide (**3d**) with 0.30 mL (2.9 mmol) of diethylamine in 20 mL of CH_2Cl_2 for 6 h at rt, followed by chromatography with the solvent mixture used for the separation of **5a** gave 34 mg (26%) of **5d**.

4-(Di-*n*-propylamino)-5-[(3-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (5e). The reaction of 404 mg (1.48 mmol) of 4-chloro-5-[(3-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (**1a**) with 1.8 mL (13 mmol) of di-*n*-propylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (10:1), gave 28 mg of an unknown mixture. Elution with the same solvent mixture (4:1) afforded 234 mg (47%) of **5e**: yellowish red oil; ^{1}H NMR δ 0.91 (t, J = 7 Hz, 6H), 1.43–1.97 (m, 4H), 3.62 (t, J = 7 Hz, 4H), 7.30–8.16 (m, 4H); IR (neat) 2960, 1586, 1528, 1350 cm^{-1}; MS (*m/z*) 338 (M$^+$). Anal. Calcd for $C_{14}H_{18}N_4O_2S_2$: C, 49.69; H, 5.36; N, 16.55; S, 18.95. Found: C, 49.82; H, 5.37; N, 16.59; S, 19.01.

5-[(4-Chloro-3-nitrophenyl)imino]-4-(di-*n*-propylamino)-5*H*-1,2,3-dithiazole (5f). The reaction of 438 mg (1.42 mmol) of 4-chloro-5-[(4-chloro-3-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (**1c**) with 1.1 mL (8.0 mmol) of di-*n*-propylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (10:1), gave 15 mg of an unknown mixture. Elution with the same solvent mixture (4:1) gave 396 mg (75%) of **5f**: yellowish red oil; ^{1}H NMR δ 0.90 (t, J = 7 Hz, 6H), 1.43–1.94 (m, 4H), 3.59 (t, J = 7 Hz, 4H), 7.24 (dd, J = 9, 2 Hz, 1H), 7.58 (d, J = 9 Hz, 1H), 7.62 (d, J = 2 Hz, 1H); IR (neat) 2960, 1584, 1530, 1350 cm^{-1}; MS (*m/z*) 372 (M$^+$). Anal. Calcd for $C_{14}H_{17}ClN_4O_2S_2$: C, 45.09; H, 4.60; N, 15.03; S, 17.20. Found: C, 45.35; H, 4.66; N, 15.01; S, 17.19.

4-(Di-*n*-propylamino)-5-[(4-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (5g). The reaction of 630 mg (2.30 mmol) of 4-chloro-5-[(4-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (**1b**) with 1.5 mL (11 mmol) of di-*n*-propylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (4:1), gave 38 mg of an unknown mixture. Elution with the same solvent mixture (4:1) gave 465 mg (60%) of **5g**: red oil; ^{1}H NMR δ 0.90 (t, J = 7 Hz, 6H), 1.43–1.97 (m, 4H), 3.61 (t, J = 7 Hz, 4H), 7.17 (d, J = 9 Hz, 2H), 8.31 (d, J = 9 Hz, 2H); IR (neat) 2970, 1580, 1518, 1340 cm^{-1}; MS (*m/z*) 338 (M$^+$). Anal. Calcd for $C_{14}H_{18}N_4O_2S_2$: C, 49.69; H, 5.36; N, 16.55; S, 18.95. Found: C, 49.79; H, 5.40; N, 16.59; S, 19.00.

5-[(2-Chloro-5-nitrophenyl)imino]-4-(di-*n*-propylamino)-5*H*-1,2,3-dithiazole (5h). The reaction of 405 mg (1.31 mmol) of 4-chloro-5-[(2-chloro-5-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (**1d**) with 1.0 mL (7.3 mmol) of di-*n*-propylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (5:1), gave 16 mg of an unknown mixture. Elution with the same solvent mixture (5:2), gave 374 mg (76%) of **5h**, which was recrystallized from *n*-hexane: mp 60–61 °C; ^{1}H NMR δ 0.90 (t, J = 7 Hz, 6H), 1.45–1.96 (m, 4H), 3.64 (t, J = 7 Hz, 4H), 7.55–7.74 (m, 1H), 7.90–8.06 (m, 2H); IR (neat) 2960, 1585, 1523, 1345, 1060 cm^{-1}; MS (*m/z*) 372 (M$^+$). Anal. Calcd for $C_{14}H_{17}ClN_4O_2S_2$: C, 45.09; H, 4.60; N, 15.03; S, 17.20. Found: C, 45.27; H, 4.68; N, 15.04; S, 17.27.

5-[(4-Bromophenyl)imino]-4-(di-*n*-propylamino)-5*H*-1,2,3-dithiazole (5i). The reaction of 507 mg (1.65 mmol) of 5-[(4-bromophenyl)imino]-4-chloro-5*H*-1,2,3-dithiazole (**1e**) with 1.3 mL (9.5 mmol) of di-*n*-propylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (10:1), gave 22 mg of an unknown mixture. Elution with the same solvent mixture (4:1) gave 372 mg of a crude **5i**, which was purified on HPLC to yield 361 mg (59%) of **5i**. Compound **5i** was recrystallized from a mixture of methanol and CH_2Cl_2: mp 31–32 °C; ^{1}H NMR δ 0.90 (t, J = 7 Hz, 6H), 1.30–2.06 (m, 4H), 3.60 (t, J = 7 Hz, 4H), 6.97 (d, J = 9 Hz, 2H), 7.56 (d, J = 9 Hz, 2H); IR (neat) 2960, 2930, 1590, 1527, 1480 cm^{-1}; MS (*m/z*) 371 (M$^+$). Anal. Calcd for $C_{14}H_{18}BrN_3S_2$: C, 45.16; H, 4.87; N, 11.29; S, 17.22. Found: C, 45.27; H, 4.89; N, 11.35; S, 17.51.

4-(Di-*n*-propylamino)-5-[(4-methoxyphenyl)imino]-5*H*-1,2,3-dithiazole (5j). The reaction of 476 mg (1.84 mmol) of 4-chloro-5-[(4-methoxyphenyl)imino]-5*H*-1,2,3-dithiazole (**1f**) with 3.0 mL (22 mmol) of di-*n*-propylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (10:1), gave 75 mg of an unknown mixture. Elution with the same solvent mixture (5:1) afforded 139 mg (23%) of **5j**: yellowish red oil; ^{1}H NMR δ 0.93 (t, J = 7 Hz, 6H), 1.30–2.10 (m, 4H), 3.63 (t, J = 7 Hz, 4H), 3.85 (s, 3H), 6.97 (d, J = 9 Hz, 2H), 7.23 (d, J = 9 Hz, 2H); IR (neat) 2955, 1578, 1500, 1242 cm^{-1}; MS (*m/z*) 323 (M$^+$). Anal. Calcd for $C_{15}H_{21}N_3OS_2$: C, 55.70; H, 6.54; N, 12.99; S, 19.82. Found: C, 55.77; H, 6.59; N, 12.97; S, 19.78.

4-(Di-*n*-propylamino)-5-[(4-methylphenyl)imino]-5*H*-1,2,3-dithiazole (5k). The reaction of 542 mg (2.23 mmol) of 4-chloro-5-[(4-methylphenyl)imino]-5*H*-1,2,3-dithiazole (**1g**) with 1.8 mL (13 mmol) of di-*n*-propylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (5:1), gave 125 mg (18%) of **5k**: yellowish red oil; ^{1}H NMR δ 0.94 (t, J = 7 Hz, 6H), 1.30–2.07 (m, 4H), 2.43 (s, 3H), 3.65 (t, J = 7 Hz, 4H), 7.10 (d, J = 9 Hz, 2H), 7.35 (d, J = 9 Hz, 2H); IR (neat) 2960, 1582, 1528, 1504 cm^{-1}; MS (*m/z*) 307 (M$^+$). Anal. Calcd for $C_{15}H_{21}N_3S_2$: C, 58.60; H, 6.88; N, 13.67; S, 20.85. Found: C, 58.32; H, 6.70; N, 13.55; S, 20.43.

4-[Di-(2-propenyl)amino]-5-[(4-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (5l). The reaction of 430 mg (1.57 mmol) of 4-chloro-5-[(4-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (**1b**) with 1.5 mL (12 mmol) of diallylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (10:1), gave 118 mg of an unknown mixture. Elution with the same solvent mixture (4:1) gave 104 mg (20%) of **5l**: dark red oil; ^{1}H NMR δ 4.27 (d, J = 6 Hz, 4H), 5.00–5.40 (m, 4H, 2C=CH$_2$), 5.70–6.23 (m, 2H, 2CH=C), 7.18 (d, J = 9 Hz, 2H), 8.30 (d, J = 9 Hz, 2H); IR (neat) 1580, 1510, 1340 cm^{-1}; MS (*m/z*) 334 (M$^+$). Anal. Calcd for $C_{14}H_{14}N_4O_2S_2$: C, 50.28; H, 4.22; N, 16.75; S, 19.17. Found: C, 50.25; H, 4.32; N, 16.59; S, 19.15.

5-[(4-Chloro-3-nitrophenyl)imino]-4-(di-*n*-butylamino)-5*H*-1,2,3-dithiazole (5m). The reaction of 363 mg (1.18 mmol) of 4-chloro-5-[(4-chloro-3-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (**1c**) with 1.2 mL (7.1 mmol) of di-*n*-butylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (10:1), gave 31 mg of an unknown mixture. Elution with the same solvent mixture (4:1) gave 297 mg (63%) of **5m**: yellowish red oil; ^{1}H NMR δ 0.75–1.09 (m, 6H), 1.09–1.90 (m, 8H), 3.64 (t, J = 7 Hz, 4H), 7.24 (dd, J = 9, 2 Hz, 1H), 7.58 (d, J = 9 Hz, 1H), 7.62 (d, J = 2 Hz, 1H); IR (neat) 2975, 1585, 1534, 1474, 1352 cm^{-1}; MS (*m/z*) 400 (M$^+$). Anal. Calcd for $C_{16}H_{21}ClN_4O_2S_2$: C, 47.93; H, 5.28; N, 13.97; S, 15.99. Found: C, 47.95; H, 5.27; N, 14.01; S, 15.89.

4-(Di-*n*-butylamino)-5-[(4-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (5n). The reaction of 419 mg (1.53 mmol) of 4-chloro-5-[(4-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (**1b**) with 1.5 mL (8.9 mmol) of di-*n*-butylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (10:1), gave 29 mg of an unknown mixture. Elution with the same solvent mixture (4:1) afforded 353 mg (63%) of **5n**: dark red oil; ^{1}H NMR δ 0.80–1.10 (m, 6H), 1.10–1.90 (m, 8H), 3.65 (t, J = 7 Hz, 4H), 7.16 (d, J = 9 Hz, 2H), 8.30 (d, J = 9 Hz, 2H); IR (neat) 2944, 1575, 1508, 1332 cm^{-1}; MS (*m/z*) 366 (M$^+$). Anal. Calcd for $C_{16}H_{22}N_4O_2S_2$: C, 52.44; H, 6.05; N, 15.29; S, 17.50. Found: C, 52.39; H, 6.08; N, 15.25; S, 17.61.

5-[(4-Bromophenyl)imino]-4-(di-*n*-butylamino)-5*H*-1,2,3-dithiazole (5o). The reaction of 405 mg (1.43 mmol) of 5-[(4-bromophenyl)imino]-4-chloro-5*H*-1,2,3-dithiazole (**1e**) with 1.5 mL (8.9 mmol) of di-*n*-butylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (10:1), gave 22 mg of an unknown mixture. Elution with the same solvent mixture (5:1) gave 325 mg (59%) of **5o**: yellowish red oil; ^{1}H NMR δ 0.80–1.10 (m, 6H), 1.10–1.90 (m, 8H), 3.64 (t, J = 7 Hz, 4H), 6.97 (d, J = 9 Hz, 2H), 7.53 (d, J = 9 Hz, 2H); IR (neat) 2960, 1592, 1530, 1482 cm^{-1}; MS (*m/z*)

399 (M^+). Anal. Calcd for $C_{16}H_{22}BrN_3S_2$: C, 48.00; H, 5.54; N, 10.49; S, 16.01. Found: C, 48.10; H, 5.56; N, 10.45; S, 16.12.

4-(Diisobutylamino)-5-[(4-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (5p). The reaction of 421 mg (1.54 mmol) of 4-chloro-5-[(4-nitrophenyl)imino]-5*H*-1,2,3-dithiazole (**1b**) with 1.8 mL (10 mmol) of diisobutylamine in 30 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (10:1), gave 85 mg of an unknown mixture. Elution with the same solvent mixture (5:1) gave 52 mg of crude product **5p**, which was separated by HPLC to give 42 mg (7%) of **5p**: red oil; ^1H NMR δ 0.89 (d, J = 7 Hz, 12H), 1.75–2.32 (m, 2H), 3.57 (d, J = 7 Hz, 4H), 7.15 (d, J = 9 Hz, 2H), 8.31 (d, J = 9 Hz, 2H); IR (neat) 2960, 1580, 1518, 1340 cm^{-1}; MS (*m/z*) 366 (M^+). Anal. Calcd for $C_{16}H_{22}N_4O_2S_2$: C, 52.44; H, 6.05; N, 15.29; S, 17.50. Found: C, 52.40; H, 6.11; N, 15.23; S, 17.41.

5-[(4-Methylphenyl)imino]-4-(pentane-1,5-diylamino)-5*H*-1,2,3-dithiazole (5q). The reaction of 500 mg (2.06 mmol) of 4-chloro-5-[(4-methylphenyl)imino]-5*H*-1,2,3-dithiazole (**1g**) with 0.60 mL (6.1 mmol) of piperidine in 20 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (3:1), gave 105 mg of unknown mixtures. Elution with the same solvent mixture (1:1) gave 198 mg of another mixture, which was rechromatographed to give 83 mg (14%) of **5q**: yellow oil; ^1H NMR δ 1.45–1.85 (m, 6H), 2.30 (s, 3H), 3.36–3.75 (m, 4H), 6.83 (d, J = 8 Hz, 2H), 7.05 (d, J = 8 Hz, 2H); IR (neat) 2930, 1580, 1501, 1252 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, 57.45; H, 5.76; N, 14.29; S, 22.16. Elution next with CH_2Cl_2 (150 mL) and a mixture of CH_2Cl_2 and Et_2O (5:1, 50 mL) afforded 203 mg (1.00 mmol, 49%) of *N'*-(4-methylphenyl)-*N,N*-(pentane-1,5-diyl)cyanoformamidine and 45 mg (0.192 mmol, 9%) of *N*-(4-methylphenyl)-*N',N'*-(pentane-1,5-diyl)thiourea, respectively.[4]

4-(Hexane-1,5-diylamino)-5-[(4-methylphenyl)imino]-5*H*-1,2,3-dithiazole (5r). The reaction of 461 mg (1.90 mmol) of 4-chloro-5-[(4-methylphenyl)imino]-5*H*-1,2,3-dithiazole (**1g**) with 1.5 mL (13 mmol) of 2-methylpiperidine in 20 mL of CH_2Cl_2, followed by chromatography with a mixture of petroleum ether and CH_2Cl_2 (10:1), gave 55 mg of an unknown mixture. Elution with the same solvent mixture (5:1) gave 89 mg (15%) of **5r**: yellow oil; ^1H NMR δ 1.24 (d, J = 7 Hz, 3H), 1.37–2.07 (m, 6H), 2.36 (s, 3H), 3.00–3.45 (m, 1H), 3.97–4.33 (m, 1H), 4.73–5.13 (m, 1H), 7.03 (d, J = 8 Hz, 2H), 7.23 (d, J = 8 Hz, 2H); IR (neat) 2923, 1577, 1499 cm^{-1}; MS (*m/z*) 305 (M^+). Anal. Calcd for $C_{15}H_{19}N_3S_2$: C, 58.98; H, 6.27; N, 13.76; S, 20.99. Found: C, 58.70; H, 6.08; N, 13.67; S, 20.55.

[(2-Chloro-5-nitrophenyl)imino]cyanomethyl diethylamino disulfide (3d) was prepared by the literature procedures:[4] ^1H NMR δ 1.22 (t, J = 7 Hz, 6H), 3.12 (q, J = 7 Hz, 4H), 7.54–8.17 (m, 3H); IR (neat) 2250 (C≡N); MS (*m/z*) 344 (M^+). Anal. Calcd for $C_{12}H_{13}N_4ClO_2S_2$: C, 41.80; H, 3.80; N, 16.25; S, 18.59. Found: C, 42.02; H, 3.79; N, 16.30; S, 18.87.

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