Unusually Facile Ring-Opening Reaction in the Pyridine System

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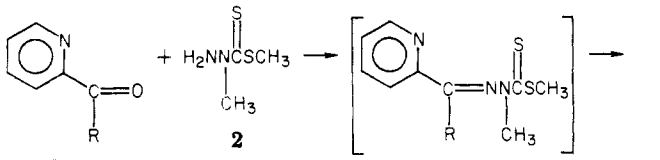
Reaction of 2-acetylpyridine with methyl 1-methylhydrazinecarbodithioate (**2**) resulted in formation of methyl (*E,Z,E*)-[4-(3,4-dihydro-2,6-dimethyl-3-thioxo-1,2,4-triazin-5(2*H*)-ylidene)-2-butenylidene]methylhydrazinecarbodithioate (**4b**) rather than the expected hydrazone, **3b**. Reaction of pyridine-2-carboxaldehyde with **2**, however, gave mostly the corresponding hydrazone **3a** and some triazine **4a**. Alkylation of **4a** and **4b** with iodomethane afforded the 3-methylthio derivatives **8a** and **8b**, respectively. The structure of **8a** was determined by ^{1}H NMR spectrometry and confirmed by a single-crystal X-ray analysis. Reaction of hydrazone **3b** with **2** gave **4b**, while treatment of **3b** with dimethylamine afforded 6-(dimethylamino)-3,6-dihydro-1,3-dimethyl-4*H*-pyrido[1,2-*d*]-[1,2,4]triazine-4-thione (**14a**). Alkylation of **14a** with iodomethane in aqueous base resulted in the formation of (*Z,E*)-4-[2,6-dimethyl-3-(methylthio)-1,2,4-triazin-5(2*H*)-ylidene]-2-butenal (**15**). Reaction of aldehyde **15** with **2** gave **4b**.

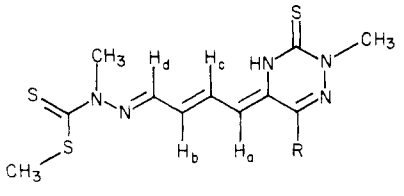
In the course of our investigation of the chemotherapeutic properties of 2-acetylpyridine 3-thiosemicarbazones, we required methyl 3-[1-(2-pyridyl)ethylidene]methylhydrazinecarbodithioate (**3b**) as a possible intermediate for the preparation of 2-acetylpyridine N^2-methyl-3-thiosemicarbazones. Because methyl 1-methylhydrazinecarbodithioate (**2**) has been shown to react with a wide variety of aldehydes and ketones (formaldehyde, acetaldehyde, benzaldehyde,[1] furfural,[2] 2-acetylfuran,[3] isatin,[4] pyridine-2-carboxaldehyde,[5] 6-methylpyridine-2-carboxaldehyde[6]) to give the expected hydrazones, we felt that condensation of 2-acetylpyridine (**1b**) with carbodithioate **2** should proceed in the normal fashion to give hydrazone **3b**. However, **3b** could not be prepared this way. Instead, the reaction proceeded with the evolution of methyl mercaptan to afford an orange, high melting, insoluble product, **4b**, with an empirical formula of $C_{12}H_{17}N_5S_3$. In this article we describe the identification of this novel product as methyl (*E,Z,E*)-[4-(3,4-dihydro-2,6-dimethyl-3-thioxo-1,2,4-triazin-5(2*H*)-ylidene)-2-butenylidene]-methylhydrazinecarbodithioate and propose a mechanism to account for its formation.



1a, R = H
b, R = CH_3

2

3a, R = H
b, R = CH_3



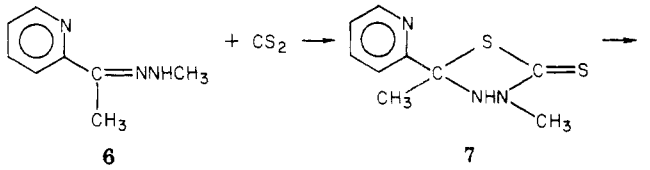
4a, R = H
b, R = CH

Examination of the course of the reaction revealed that no perceptible change occurred until the addition of a catalytic amount of glacial acetic acid. At this point, reaction commenced, as evidenced by the evolution of methyl mercaptan and the formation of **4b**. Analysis of the reaction mixture showed no formation of **3b** prior to the addition of acid, even following 3 h at reflux. Following the addition of catalyst, a trace of **3b** could be detected. Under identical conditions, 2-acetyl-6-methylpyridine, 2-acetylquinoline, and acetophenone afforded only the corresponding Schiff bases (**5a-c**, respectively). Pyridine-2-carboxaldehyde gave predominately methyl 3-(2-pyridylmethylene)methylhydrazinecarbodithioate (**3a**) accompanied by a lesser amount of methyl (*E,Z,E*)-[4-(3,4-dihydro-2-methyl-3-thioxo-1,2,4-triazin-5(2*H*)-ylidene)-2-butenylidene]methylhydrazinecarbodithioate (**4a**, $C_{11}H_{17}N_5S_3$).

$CH_3C(R)=O + H_2NN(CH_3)C(S)SCH_3 \rightarrow CH_3C(R)=NN(CH_3)C(S)SCH_3$

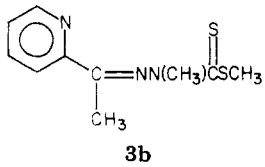
5a, R = 2-(6-methylpyridyl)
5b, R = 2-quinolinyl
5c, R = phenyl

The synthesis of **3b** and its reaction with **2** were undertaken in order to determine whether **3b** was an intermediate in the formation of **4b**. Reaction of 2-acetylpyridine (**1b**) with methylhydrazine and condensation of the resulting hydrazone **6** with carbon disulfide gave 3,5-dimethyl-5-(2-pyridyl)-1,3,4-thiadiazolidine-2-thione (**7**). Sandström[7] and Anthoni et al.[8] have shown that alkylation



6

7



3b

(1) Sandstrom, J. *Ark. Kemi* **1956**, *10*, 255.
(2) Serban, A. W.; Burridge, B.; Alcock, K. T. U.S. Patent 4 064 262, 1977; *Chem. Abstr.* **1978**, *88*, 120967.
(3) French Demande 2 306 205, 1976; *Chem. Abstr.* **1977**, *87*, 39206.
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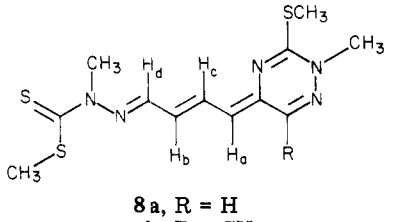
(6) Akbar Ali, M.; Livingstone, S. E.; Phillips, D. J. *Inorg. Chem. Acta* **1972**, *6*, 39.
(7) Sandström, J. *Acta Chem. Scand.* **1963**, *17*, 937.
(8) Anthoni, A.; Larsen, C.; Nielson, P. H. *Acta Chem. Scand.* **1970**, *24*, 197.

of these thiones with iodomethane in aqueous base affords methyl 3-alkylidenemethylhydrazinecarbodithioates. Alkylation of **7** gave **3b**, which proved to be a suprisingly unstable oil. The NMR spectrum of **3b** clearly shows an intact pyridine ring system. The lowest field proton, H-5, appears as a broad doublet at δ 8.70. An absorbance at δ 8.25 is assigned to H-3, while the H-4 proton is an apparent triplet of doublets at δ 7.82. Singlets with chemical shifts of δ 3.77, 2.5 and 2.48 may be assigned to the *N*-methyl, *S*-methyl, and *C*-methyl groups, respectively.

Reaction of **3a,b** with **2** led to the formation of **4a,b**. These compounds proved to be insoluble in the usual organic solvents but were soluble in pyridine or methanolic sodium hydroxide. The solubility properties of **4a,b** suggested that the molecules contained a NHC(=S) moiety.

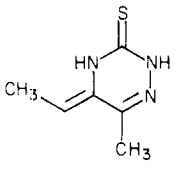
The NMR spectrum (220 MHz, Me_2SO-d_6) of **4b** was not consistent with aromaticity and indicated that the product was a conjugated olefin. The high-field absorbance of **4b** shows a multiplet of two protons (H_d, H_c) centered at δ 7.75. This multiplet consists of a doublet for H_d (J = 9 Hz) at δ 7.79 overlapping a doublet of doublets for H_c. One of the coupling constants of H_c is readily seen to be 13 Hz. A doublet of doublets at δ 6.45 (J_{bd} = 9 Hz, J_{bc} = 16 Hz) may be assigned to H_b. Proton H_a appears as a doublet (J_{ac} = 13 Hz) at δ 5.73. The high coupling constant of 16 Hz suggests that H_b and H_c are separated by a trans double bond.

Transformation of thioamides **4a,b** to their *S*-methyl derivatives **8a,b** was accomplished by treatment with iodomethane in methanolic sodium hydroxide.



8 a, R = H
b, R = CH_3

Adams and Shepard[9] demonstrated an unusual tautomeric effect upon an alkyl group at the 5-position in the 1,2,4-triazine series. Cyclization of 2,3-pentanedione thiosemicarbazone with aqueous sodium hydroxide afforded 5-ethylidene-6-methyl-3-thioxo-2,3,4,5-tetrahydro-1,2,4-triazine (**9**). They confirmed the stereochemistry by



9

X-ray analysis.[9] This suggested that **4a,b** and **8a,b** should have the stereochemistry that we have indicated, and this expectation was confirmed by a single-crystal X-ray analysis of **8a**. An ORTEP plot of the refined structure is presented in Figure 1. The packing diagram for the unit cell is shown in Figure 2 (see the paragraph at the end of the paper regarding supplementary material).

The rearrangement of a pyridine ring to a conjugated olefinic system under these mild conditions is unusual. The ease with which nucleophilic attack occurs upon the thiocarbonyl group of **3a,b** is also remarkable. Jensen[10] has noted the exceptional stability of 1-alkyl-substituted

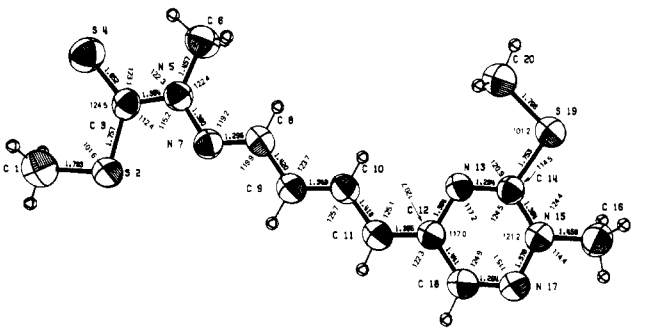
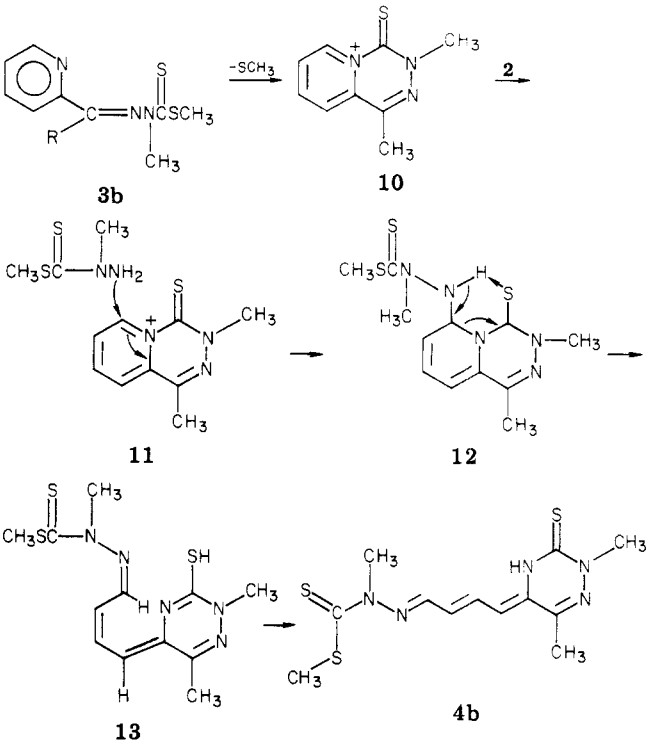


Figure 1. Molecular dimensions and crystal conformation of **8a** (ORTEP drawing).

Scheme I



hydrazinecarbodithioates such as **2**. He observed that these compounds withstood long periods of attack by aliphatic amines. We observed that methyl 1-methylhydrazinecarbodithioate (**2**) may be recovered unchanged after being heated in the atmosphere at 200 °C for 0.5 h. A mechanism to account for the formation of **4b** is detailed in Scheme I.

The formation of pyridinium intermediate **10**, followed by nucleophilic attack at the electron-deficient α-position of pyridinium salt **10** and isomerization of intermediates **12** and **13** to produce **4b**, is reminiscent of Hull's mechanism for the formation of isothiocyanatopentadienals from pyridine and thiophosgene.[11,12]

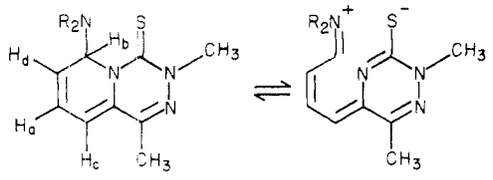
When **3b** was allowed to react with either dimethylamine or hexamethylenimine, methyl mercaptan was evolved, and deeply marroon colored products **14a** and **14b**, respectively, were isolated. The NMR spectra of these compounds indicated that the pyridine ring had been converted to a conjugated olefinic system. As the coupling constants between the four coupled protons were about 11 Hz, the absence of a trans double bond was indicated. When the chemical shifts of the corresponding protons of **14a** and

(9) Adams, J.; Shepard, R. *Tetrahedron Lett.* **1968**, 2747.
(10) Jensen, K. A.; Anthoni, A.; Kägi, B.; Larsen, C.; Pedersen, C. *Acta Chem. Scand.* **1968**, *22*, 1.
(11) Hull, R. *J. Chem. Soc. C* **1968**, 1778.
(12) Boyle, F. T.; Hull, R. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1541.

14b were compared, it was seen that H_a, H_c, and H_d had nearly identical positions in either compound, while H_b in compound **14b** was shifted upfield 0.25 ppm from the location of H_b in **14a**. This establishes H_b as geminal to the point of attachment of the amino groups.

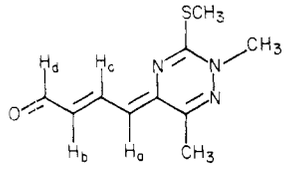
The order of coupling was established by a double-resonance experiment. Irradiation of H_d in **14a** converted H_b to a singlet and H_a to a doublet, while irradiation of H_c converted H_a to a doublet and did not affect either H_b or H_d. As H_b is geminal to the dimethylamino group, the structure of the olefinic protion of **14a** is seen to be $(CH_3)_2NCH_bCH_d{=}CH_aCH_c{=}$.

In solution, **14a,b** is orange, while crystals of the compound are deeply purple. This suggests that the predominant form in solution is the cyclized form. The purple coloration of the solid state may be explained by conversion to the dipolar form with greater extended conjugation.



14a, R,R = CH_3
b, R,R = $(CH_2)_6$

Treatment of either **14a** or **14b** with iodomethane in aqueous base gave aldehyde **15**. Reaction of this compound with **2** gave **8b**.



15

Discussion of Crystal Structure

The crystal conformation and atomic nomenclature used in the X-ray work and the molecular dimensions are shown in Figure 1. Within 0.03 Å, atoms S(2), C(8), C(9), C(10), C(11), C(12), N(13), C(14), N(15), N(17), and C(18) are coplanar. The deviations from planarity are slightly greater at the end of the chain, with atoms C(3), N(5), and N(7) being 0.08, −0.06, and −0.08 Å from the least-squares plane defined by these atoms and those in the previous list. There is thus the possiblity of an extended conjugated system, although, in the crystal, the contributions to conjugation of the atoms at the end of the chain may not be very large. Evidence for conjugation is given by the C–C, C–N, and N–N bond length which do not correspond to pure single or double bonds.[13] The two different bond lengths on the methyl-substituted sulfur atom are not unexpected since one bond will be to an sp^2 atom while the other is to an sp^3 atom.

The packing (Figure 2, supplementary material) seems quite economical of space. The only point of interest is the short S(19)–S(19) distance (3.289 Å) across a center of symmetry which may argue for a dipole–dipole or possibly a charge-transfer interaction.

Experimental Section

IR spectra were recorded on a Perkin-Elmer Model 283 grating spectrophotometer. NMR spectra were run on a Varian HR-220 spectrometer or a Varian T-60A spectrometer. Mass spectra were obtained on a Finnigan 3100D spectrometer operated in the CI mode and using methane as the reagent gas. Microanalyses were performed by Spang Microanalytical Laboratory. Melting points were determined by using a Thomas-Hoover melting point apparatus and are uncorrected.

Table I. Crystal and Experimental Data for 8a

molecular formula: $C_{12}H_{17}N_5S_3$
habit: dark red monoclinic needles, elongation along b
radiation: Cu Kα (graphite monochromator)
wavelength: 1.4318 Å
space group: (No. 9) $P2_1/c$
cell dimens (from least-squares refinement of $\pm\theta$ data)
a = 9.830 (1) Å
b = 7.438 (1) Å
c = 23.186 (3) Å
β = 101.28 (1) Å
v = 1662.51 Å^3
z = 4
mol wt: 327.48
D_m = 1.29 g cm^{-3}
D_x = 1.308 g cm^{-3}
cryst size: 0.35 × 0.2 × 0.15 mm
rflctns: 3246 (860 unobserved, 1δ)
max (sin θ)/λ: 0.61 Å^{-1}
diffractometer: Nonius CAD-4
least-squares weighting: after Peterson and Levy[16]
function minimized: $\Sigma w\Delta^2$
anisotropic temp factor: $\exp[-2\pi^2(\Sigma_i\Sigma_j U_{ij}a_i{*}a_j{*}h_ih_j)]$

X-ray Analysis. Crystallographic details for compound **8a** are given in Table I. The phase problem was solved by using MULTAN 78.[14] The XRAY 72[15] system was used for refinement of the model from MULTAN 78 with scattering factors as provided. Standard cycles of least-squares refinement and difference maps allowed recognition of all hydrogen atoms. The structure was refined to an R factor of 4.0% (observed reflections only) with anisotropic thermal parameters for the heavier atoms and isotropic parameters for the hydrogen atoms. The final bond lengths and angles are shown in Figure 1 and the atomic parameters in Table II (supplementary material). A table of observed and calculated structure factors was provided for the use of the referees and may be obtained from J.V.S.

Methyl 3-[1-(2-Pyridyl)ethylidene]methylhydrazinecarbodithioate (3b). A solution consisting of 2.25 g (10 mmol) of 3,5-dimethyl-5-(2-pyridyl)-1,3,4-thiazolidine-2-thione (**7**) and 600 mg (15 mol) of NaOH in 10 mL of 50% aqueous MeOH was treated with 1.42 g (10 mmol) of iodomethane. A yellow oil separated immediately. Stirring was continued for 1 h. The reaction mixture was extracted with $CHCl_3$ (3 × 20 mL), the $CHCl_3$ solution was dried ($MgSO_4$), and the solvent was removed under reduced pressure. This afforded 1.97 g (82%) of a pale yellow oil: IR (neat) 3070, 3000, 2935, 1617, 1589, 1573, 1472, 1430, 1360, 1250, 1210, 1103, 1050, 997, 960, 870, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.77 (d d, 1 H), 8.30 (d, 1 H), 7.67 (t d, 1 H), 7.43 (m, 1 H), 3.77 (s, 3 H, N-CH_3), 2.57 (s, 3 H, S-CH_3), 2.48 (s, 3 H, C-CH_3).

Elemental analysis was not performed on this compound due to its instability.

Methyl (*E,Z,E*)-[4-(3,4-Dihydro-2-methyl-3-thioxo-1,2,4-triazin-5(2*H*)-ylidene)-2-butenylidene]methylhydrazinecarbodithioate (4a). Method A. A solution of 6.5 g (0.048 mol) of methyl 1-methylhydrazinecarbodithioate (**2**) and 3.09 g (0.029 mol) of pyridine-2-carboxaldehyde in 10 mL of MeOH was heated at reflux for 1 h. Filtration of the hot solution gave 100 mg (1%) of orange crystals of methyl (*E,Z,E*)-[4-(3,4-dihydro-2-methyl-3-thioxo-1,2,4-triazin-5(2*H*)-ylidene)-2-butenylidene]methylhydrazinecarbodithioate (**4a**): darkens at >200 °C, mp 210–211

(13) Macgillavry, C. H.; Rieck, G. D., Eds. "International Tables for X-ray Crystallography"; Kynoch Press: Birmingham, England, 1968; Vol III.

(14) Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; Declerq, J.-P.; Woolfson, M. M. "MULTAN 78, A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data"; Universities of York and Louvain: York, England, 1978.

(15) Stewart, J. M.; Kruger, G. J.; Ammon, H. L.; Dickinson, C.; Hall, S. R. Technical Report TR 192 1972; Computer Center, The University of Maryland: College Park, MD, 1972.

(16) Peterson, S. N.; Levy, H. A. *Acta Crystallogr.* **1957**, *10*, 70.

°C dec; IR (KBr) 3280 (br, NH), 2914, 1620, 1575, 1555, 1494, 1298, 1103, 1016, 703, 677 cm^{-1}; mass spectrum (CH_4, CI), *m/e* (relative intensity) 313 (M^+, 1), 178 (100), 177 (6), 147 (5), 91 (5), 89 (7), 88 (5), 69 (30), 68 (10).

Anal. Calcd for $C_{11}H_{15}N_5S_3$: C, 42.15; H, 4.82; N, 22.34; S, 30.69. Found: C, 42.30; H, 4.84; N, 22.29; S, 30.62.

The filtrate was chilled and the crystals which separated were collected, affording 5.7 g (88%) of methyl 3-[(2-pyridyl)-methylene]methylhydrazinecarbodithioate (**3a**): mp 104–105 °C (lit.[5] mp 104 °C); ^1H NMR ($CDCl_3$) δ 8.58 (d, 1 H, H_6), 8.08 (d, 1 H, H_3), 7.93 (s, 1 H, CH=), 7.73 (t d, 1 H, H_4), 7.28 (m, H_5), 3.97 (s, 3 H, *N*-CH_3), 2.57 (s, 3 H, SCH_3).

Method B. A solution of 2.25 g (10 mmol) of **3a** and 1.36 g (10 mmol) of **2** in 5 mL of MeCN was heated at reflux for 30 h. Filtration of the hot reaction mixture afforded 300 mg (9%) of orange needles of **4a**, mp 210–211 °C dec. The IR spectra of this compound was identical with the spectrum of a sample prepared by using method A.

Methyl (*E,Z,E*)-[4-(3,4-Dihydro-2,6-dimethyl-3-thioxo-1,2,4-triazin-5(2*H*)-ylidene)-2-butenylidene]methylhydrazinecarbodithioate (4b). Method A. A solution of 6.81 g (50 mmol) of methyl 1-methylhydrazinecarbodithioate (**2**) and 6.06 g (50 mmol) of 2-acetylpyridine in 50 mL of EtOH was treated with one drop of glacial HOAc and heated at reflux. Methyl mercaptan was evolved, and crystals soon began to appear. After 4 h the product was collected, affording 7.60 g (93%) of orange crystals, mp 199–200 °C dec. An analytical sample was prepared by crystallization from DMF: IR (KBr) 1616, 1578, 1555, 1487, 1335, 1101, 1013, 965 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 7.75 (m, 2 H), 6.45 (dd, 1 H, J = 9 Hz, J = 16 Hz), 5.73 (d, 1 H, J = 13 Hz), 3.90 (s, 3 H), 3.60 (s, 3 H), 2.45 (s, 3 H), 2.06 (s, 3 H); mass spectrum (CH_4, CI), *m/e* (relative intensity) 327 (M^+, 1), 193 (6), 192 (100), 136 (8), 119 (8), 91 (10), 89 (12), 78 (11).

Anal. Calcd for $C_{12}H_{17}N_5S_3$: C, 44.01; H, 5.23; N, 21.39; S, 29.37. Found: C, 43.95; H, 5.40; N, 21.37; S, 29.34.

Method B. A solution of 239 mg (1 mmol) of **3b** in 5 mL of MeCN was treated with 136 mg (1 mmol) of **2** and the reaction mixture heated at reflux for 3 h. The solution was allowed to stand overnight, and 220 mg (67%) of orange crystals of **4b** was collected; mp 200–202 °C dec. The IR spectrum of this compound was identical with that of **4b** prepared by method A.

Methyl 3-[1-(6-Methyl-2-pyridyl)ethylidene]methylhydrazinecarbodithioate (5a). A solution of 1.35 g (10 mmol) of 2-acetyl-6-methylpyridine and 1.36 g (10 mmol) of methyl 1-methylhydrazinecarbodithioate in 5 mL of EtOH was treated with a few drops of glacial HOAc and heated at reflux for 20 h. The solution was evaporated to dryness under reduced pressure and the residue extracted into 30 mL of hexane. The solution was washed with H_2O (3 × 50 mL) and dried ($MgSO_4$), and the solvent was removed under reduced pressure. This afforded 2.01 g (79%) of a faintly brownish oil: IR (neat) 3060, 2960, 2920, 1617, 1575, 1435, 1355, 1202, 955, 795 cm^{-1}; ^1H NMR δ 8.00 (d, 1 H), 7.63 (t, 1 H), 7.23 (d, 1 H), 3.77 (s, 3 H, *N*-CH_3), 2.63 (s, 3 H), 2.60 (s, 3 H), 2.48 (s, 3 H).

Anal. Calcd for $C_{11}H_{15}N_3S_2$: C, 52.17; H, 5.97; N, 16.58; S, 25.31. Found: C, 52.20; H, 5.88; N, 16.54; S, 25.39.

Methyl 3-[1-(2-Quinolinyl)ethylidene]methylhydrazinecarbodithioate (5b). A solution of 1.71 g (10 mmol) of 2-acetylquinoline and 1.36 g (10 mmol) of methyl 1-methylhydrazinecarbodithioate (**2**)[6] in 5 mL of EtOH was treated with a few drops of glacial HOAc and heated at reflux for 10 h. The solution was chilled, and the crystals were collected, affording 2.04 g (71%) of light yellow needles (mp 91 °C) unchanged upon recrystallization from MeCN: IR (KBr) 1617, 1603, 1320, 1128, 1096, 960, 855, 848, 774, 761 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.33–7.40 (m, 6 H), 3.80 (s, 3 H, *N*-CH_3), 2.58 (s, 6 H).

Anal. Calcd for $C_{14}H_{15}N_3S$: C, 58.10; H, 5.92; N, 14.52; S, 22.16. Found: C, 57.91; H, 5.33; N, 14.60; S, 21.93.

Methyl 3-(1-Phenylethylidene)methylhydrazinecarbodithioate (5c). A solution of 2.40 g of acetophenone and 2.72 g (20 mmol) of **2** in 5 mL of EtOH was treated with a few drops of glacial HOAc and heated at reflux for 20 h. The solution was chilled and the product collected. Crystallization from MeOH afforded 1.5 g (32%) of colorless crystals of **5c**: mp 78–79 °C; IR (KBr) 1600, 1571, 1470, 1447, 1364, 1307, 1195, 1095, 1025, 953, 875, 869, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.10–7.77 (m, 2 H), 7.67–7.17 (m, 3 H), 3.70 (s, 3 H), 2.57 (s, 3 H), 2.32 (s, 3 H).

Anal. Calcd for $C_{11}H_{14}N_2S_2$: C, 55.43; H, 5.92; N, 11.75; S, 26.90. Found: C, 55.45; H, 5.90; N, 11.78; S, 26.94.

3,5-Dimethyl-5-(2-pyridyl)-1,3,4-thiadiazolidine-2-thione (7). A solution of 14 g (0.116 mol) of 2-acetylpyridine in 15 mL of MeCN was treated with 4.8 g (0.10 mol) of 98% methylhydrazine, and the mixture was heated at reflux for 1 h. The solution was cooled, treated with 10 mL of CS_2, and heated at reflux for 1 h. The reaction mixture was chilled, and the product was collected and washed with cold MeCN. Recrystallization from MeCN afforded 14 g (62%) of stout, colorless prisms: mp 124–125 °C; IR (KBr) 3120, 3003, 2975, 2930, 1585, 1574, 1497, 1467, 1432, 1377, 1110, 1046, 1037, 780, 755, 664 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.57 (d, 1 H), 7.67 (t d, 1 H), 7.43–7.10 (m, 2 H), 7.00 (s, 1 H, NH), 3.62 (s, 3 H), 2.05 (s, 3 H).

Anal. Calcd for $C_9H_{11}N_3S_2$: C, 47.97; H, 4.92; N, 18.65; S, 28.46. Found: C, 48.14; H, 4.89; N, 18.56; S, 28.38.

Methyl (*E,Z,E*)-[4-(2-Methyl-3-(methylthio)-1,2,4-triazin-5(2*H*)-ylidene)-2-butenylidene]methylhydrazinecarbodithioate (8a). A solution of 300 mg (0.96 mmol) of methyl (*E,Z,E*)-[4-(3,4-dihydro-2-methyl-3-thioxo-1,2,4-triazin-5(2*H*)-ylidene)-2-butenylidene]methylhydrazinecarbodithioate (**4a**) in 10 mL of methanolic NaOH (5 mL of 50% aqueous NaOH plus 5 mL of MeOH) was treated with 1.5 mL of (3.42 g, 24 mmol) of iodomethane. A red solid separated and was collected. Crystallization from MeCN afforded 280 mg (89%) of deep red, cubic crystals: mp 194–195 °C; IR (KBr) 3040, 2935, 1565, 1509, 1395, 1315, 1156, 1101, 1008, 701, 605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.67 (d, 1 H, J = 10 Hz), 7.36 (dd, 1 H, J = 12, 17 Hz), 7.05 (s, 1 H), 6.39 (dd, 1 H, J = 10, 17 Hz), 5.39 (d, 1 H, J = 12 Hz), 3.91 (s, 3 H), 3.42 (s, 3 H), 2.55 (s, 3 H), 2.50 (s, 3 H); mass spectrum (CH_4, CI), *m/e* (relative intensity) 328 (M + 1, 10), 327 (M, 25), 312 (10), 208 (10), 207 (61), 206 (100), 147 (77), 91 (37), 88 (63).

Anal. Calcd for $C_{12}H_{17}N_5S_3$: C, 44.01; H, 5.23; N, 21.39; S, 29.37. Found: C, 44.07; H, 5.24; N, 21.45; S, 29.45.

Methyl (*E,Z,E*)-[4-[2,6-Dimethyl-3-(methylthio)-1,2,4-triazin-4(2*H*)-ylidene]-2-butenylidene]methylhydrazinecarbodithioate (8b). A solution of 0.5 g (1.53 mmol) of methyl (*E,Z,E*)-[4-(3,4-dihydro-2,6-dimethyl-3-thioxo-1,2,4-triazin-5-(2*H*)-ylidene)-2-butenylidene]methylhydrazinecarbodithioate (**4b**) in 50 mL of ethanolic NaOH (10 mL of 50% aqueous NaOH plus 40 mL of EtOH) was treated with 1.5 mL (3.42 g, 24 mmol) of iodomethane. An orange solid separated immediately and was collected. Crystallization of the product from MeCN afforded 400 mg (76%) of orange needles of **8b**: mp 207 °C dec; IR (KBr) 3002, 2937, 2920, 1606, 1595, 1570, 1525, 1466, 1412, 1390, 1369, 1307, 1116, 1013, 971, 862 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.70 (d, 1 H, J = 10 Hz), 7.52 (dd, 1 H J = 10, 15 Hz), 6.43 (dd, 1 H, J = 10, 15 Hz), 5.54 (d, 1 H, J = 10 Hz), 3.93 (s, 3 H), 3.45 (s, 3 H), 2.54 (s, 3 H), 2.52 (s, 3 H), 2.00 (s, 3 H).

Anal. Calcd for $C_{13}H_{19}N_5S_3$: C, 45.72; H, 5.61; N, 20.51; S, 28.17. Found: C, 45.81; H, 5.55; N, 20.54; S, 29.18.

6-(Dimethylamino)-3,6-dihydro-1,3-dimethyl-4*H*-pyrido[1,2-*d*][1,2,4]triazine-4-thione (14a). A solution of 20 g (0.084 mol) of methyl 3-[1-(2-pyridyl)ethylidene]methylhydrazinecarbodithioate (**3b**) and 13 mL (5.2 g, 0.115 mol) of 40% aqueous dimethylamine in 25 mL of MeCN was stirred at room temperature for 5 days. The product was collected and washed with MeCN, affording 7.9 g (40%) of dark maroon, irregular crystals: mp 158–162 °C; IR (KBr) 2990, 2910, 1626, 1595, 1538, 1340, 1183, 1102, 1061, 849, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.21 (t, 1 H, J = 11 Hz), 7.02 (d, 1 H, J = 11 Hz), 6.05 (d, 1 H, J = 11 Hz), 5.48 (t, 1 H, J = 11 Hz), 4.02 (s, 3 H), 3.04 (s, 3 H), 2.25 (s, 3 H).

Anal. Calcd for $C_{11}H_{16}N_4S$: C, 55.90; H, 6.82; N, 23.71; S, 13.57. Found: C, 56.13; H, 6.80; N, 23.63; S, 13.70.

6-(Hexahydro-1*H*-azepin-1-yl)-3,6-dihydro-1,3-dimethyl-4*H*-pyrido[1,2-*d*][1,2,4]triazine-4-thione (14b). A solution of 6.0 g (25 mol) of methyl 3-[1-(2-pyridyl)ethylidene]methylhydrazinecarbodithioate (**3b**) and 2.6 g (26 mmol) of hexamethyleneimine in 10 mL of MeCN was heated at reflux for 8 h. Methyl mercaptan was evolved, as evidenced by the yellow color imparted to a strip of filter paper moistened with 5% PbOAc solution. The reaction mixture was chilled, and the crystals which separated were collected. This gave 5.6 g (77%) of deeply maroon colored flat rods: mp 190–192 °C dec; IR (KBr) 2930, 1622, 1537, 1425, 1327, 1178, 1055, 1003, 855, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ

8.27 (t, 1 H, J = 12 Hz), 7.09 (d, 1 H, J = 12 Hz), 5.80 (d, 1 H, J = 12 Hz), 5.52 (t, 1 H, J = 12 Hz), 4.00 (s, 3 H), 3.41 (m, 4 H), 2.24 (s, 3 H), 2.24 (s, 3 H), 1.70 (m, 8 H).

Anal. Calcd for $C_{15}H_{24}N_4S$: C, 62.03; H, 7.64; N, 19.29; S, 11.04. Found: C, 61.80; H, 7.92; N, 19.24; S, 11.05.

(*Z*,*E*)-4-[2,6-Dimethyl-3-(methylthio)-1,2,4-triazin-5-(2*H*)-ylidene]-2-butenal (15). A solution of 250 mg (1.06 mmol) of **14a** in 10 mL of EtOH was treated with 2 mL of 10% aqueous NaOH and 2 mL (4.56 g, 32 mmol) of iodomethane. The reaction mixture was heated on a steam bath for 30 min and then diluted with 10 mL of H_2O. An oil separated which solidified upon being cooled and scratched. The product was collected and recrystallized twice from MeCN. This afforded 50 mg (22%) of orange, square plates of **15**: mp 170–171 °C; IR (KBr) 3037, 3010, 2950, 2800, 2735, 1657, 1570, 1505, 1433, 1131, 1016, 975, 859, 645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.55 (d, 1 H, 8 Hz), 8.02 (dd, 1 H, J = 12, 16 Hz), 6.13 (dd, 1 H, J = 8, 16 Hz), 5.63 (d, 1 H, J = 12 Hz), 3.52 (s, 3 H), 2.57 (s, 3 H), 2.07 (s, 3 H); mass spectrum (CH_4, CI), m/e (relative intensity) 225 (M + 2, 75), 224 (M + 1, 100), 223 (M, 63), 221 (18), 208 (17), 194 (8), 180 (13), 121 (7).

Anal. Calcd for $C_{10}H_{13}N_3OS$: C, 53.79; H, 5.87; N, 18.82; S, 14.36. Found: C, 53.86; H, 5.80; N, 18.65; S, 14.37.

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Supplementary Material Available: Crystal packing diagram of the unit cell for compound **8a** and Table II containing atomic parameters for the refined structure of **8a** (2 pages). Ordering information is given on any current masthead page.

Reactions of Polychlorobenzenes with Alkanethiol Anions in HMPA. A Simple, High-Yield Synthesis of Poly(alkylthio)benzenes

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Reactions of the isomeric trichlorobenzenes and tetrachlorobenzenes and of pentachloro- and hexachlorobenzene with an excess of the sodium salt of the isopropanethiol, in HMPA, afforded the products of complete displacement of all the chlorine atoms present in the molecule. Similar substitutions were also obtained with EtSNa. The reactions with MeSNa were in some cases complicated by the competitive nucleophilic attack at the methyl group of the initially formed aryl methyl thioethers which are thus demethylated to afford thiophenols.

In a previous paper[1] we have recently reported that nucleophilic substitutions of unactivated aryl halides by the sodium salts of thiols can be easily effected by working in hexamethylphosphoramide (HMPA). Thus, fluoro-, chloro-, bromo-, and iodobenzene react with Me_2CHSNa to give phenyl isopropyl sulfide (**1**) in good yields. Similarly, *o*-, *m*-, and *p*-dichlorobenzene give good yields of the corresponding *o*- (**2**), *m*- (**3**), and *p*-bis(isopropylthio)-benzene (**4**). These reactions have been demonstrated to

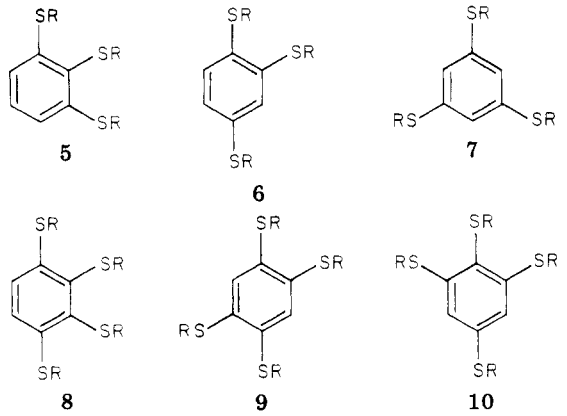
$$C_6H_5X + Me_2CHSNa \rightarrow \underset{\mathbf{1}}{C_6H_5SCHMe_2} + NaX$$

X = F, Cl, Br, I

$$o\text{-, } m\text{-, or } p\text{-}C_6H_4Cl_2 + 2Me_2CHSNa \rightarrow \underset{\mathbf{2\text{-}4}}{o\text{-, } m\text{-, or } p\text{-}C_6H_4(SCHMe_2)_2} + 2NaCl$$

occur by the classical S_NAr mechanism. It was also observed that chlorine and the $SCHMe_2$ group activate the displacement of chlorine by Me_2CHSNa.[1] On the basis of these results it can be expected that these reactions should easily occur with polychlorobenzenes, thus providing a simple method for the synthesis of poly(alkylthio)benzenes. Besides some classical, but rather tedious, procedures, the best method described in the literature to obtain aryl alkyl sulfides consists in the reaction of aryl bromide with cuprous mercaptides in quinoline at high temperature.[2,3]

Scheme I



R = Me_2CH

This procedure, however, suffers from the limitation that aromatic chloro compounds cannot be used and moreover the reaction fails when applied to polyhalogenated aromatic compounds such as 1,2,4,5-tetrabromobenzene[2,4] and penta- and hexabromobenzenes.[2]

We report in this paper the results of an investigation carried out in HMPA with polychlorobenzenes and RSNa. Excellent results were obtained with Me_2CHSNa and EtSNa which effect the complete displacement of all the chlorine atoms present in the molecule. With MeSNa

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