Pyridazines with Heteroatom Substituents in Position 3 and 5. 2 [1]. Regioselective Introduction of Mercapto Groups in Pyridazines

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The nucleophilic substitution of halogen in 3,5-dichloro-6-phenylpyridazine **1**, 5-chloro-2-methyl-6-phenylpyridazin-3(2*H*)-one **13** as well as in 3-chloro-2-methyl-6-phenylpyridazin-5(2*H*)-one **14** with methoxy, ethoxy and the 2-methyl-2-propanethiolate anion is described. In the last type of compounds the *t*-butylthio groups can be eliminated regioselectively with Lewis acids, resulting in the formation of monomercapto and monothiopyridazines.

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In continuation of our work on pyridazine chemistry, we here describe a method for regioselective introduction of a thione function in positions 3 or 5 of the 3,5-dichloro-6-phenylpyridazine **1**. The usual route to pyridazine thiones of this type is the reaction of chloropyridazines or pyridazinones with phosphorus pentasulfide in pyridine [2,3] or Lawesson's reagent [4], however these methods are not always selective as they yield completely sulfurated products. The 2-methyl-2-propanethiolate anion has been used to introduce a mercapto moiety into various heterocyclic systems [5], and it has been shown that the *t*-butyl group can be eliminated by mineral acids [6] as well as Lewis acids [7].

This reaction has been used here as a route for the regioselective introduction of mercapto groups into the following 6-phenylpyridazine derivatives **4**, **5**, **9**, **12**, **17**, **18** and **19**. These mercaptopyridazines would have been difficult to obtain with standard methods.

Results and Discussion.

The nucleophilic substitution reactions in the starting 3,5-dichloro-6-phenylpyridazine **1** were performed *via* the alkoxide using the corresponding alcohol as solvent, and in the case of the 2-methyl-3-propane thiolate anion 2-propanol was used as solvent.

By careful monitoring of the reaction conditions, it was possible to obtain the monosubstituted products, such as compounds **2** and **6**. With the methoxide anion nucleophilic substitution first takes place at positon 5 in 3,5-dichloro-6-phenylpyridazine [8]. This is also the case for the nucleophilic 2-methyl-2-propanethiolate anion as demonstrated for compound **2a** which on reaction with an equivalent of 2-methyl-2-propanethiolate anion gave a product which showed physical and spectroscopial data different from those of compound **7**, which was obtained by reacting compound **6** with an equimolar amount of methoxide anion, Scheme 1.

A side reaction was observed in the reaction of 3-chloro-5-methoxy-6-phenylpyridazine **2a**, with the 2-methyl-2-propanethiolate anion. Under a variety of reaction conditions the reaction always resulted in 3-chloro-5-hydroxy-6-phenylpyridazine **2c** as the main product, along with the expected product **3a**, which demonstrates cleavage of the methylether bond [9] under the reaction condition used thus preventing further substitution at the 3-position in the starting compound **2a**. However, in the case of 3-chloro-5-ethoxy-6-phenylpyridazine **2b**, no side reactions was observed on reaction with the 2-methyl-2-propanethiolate anion.

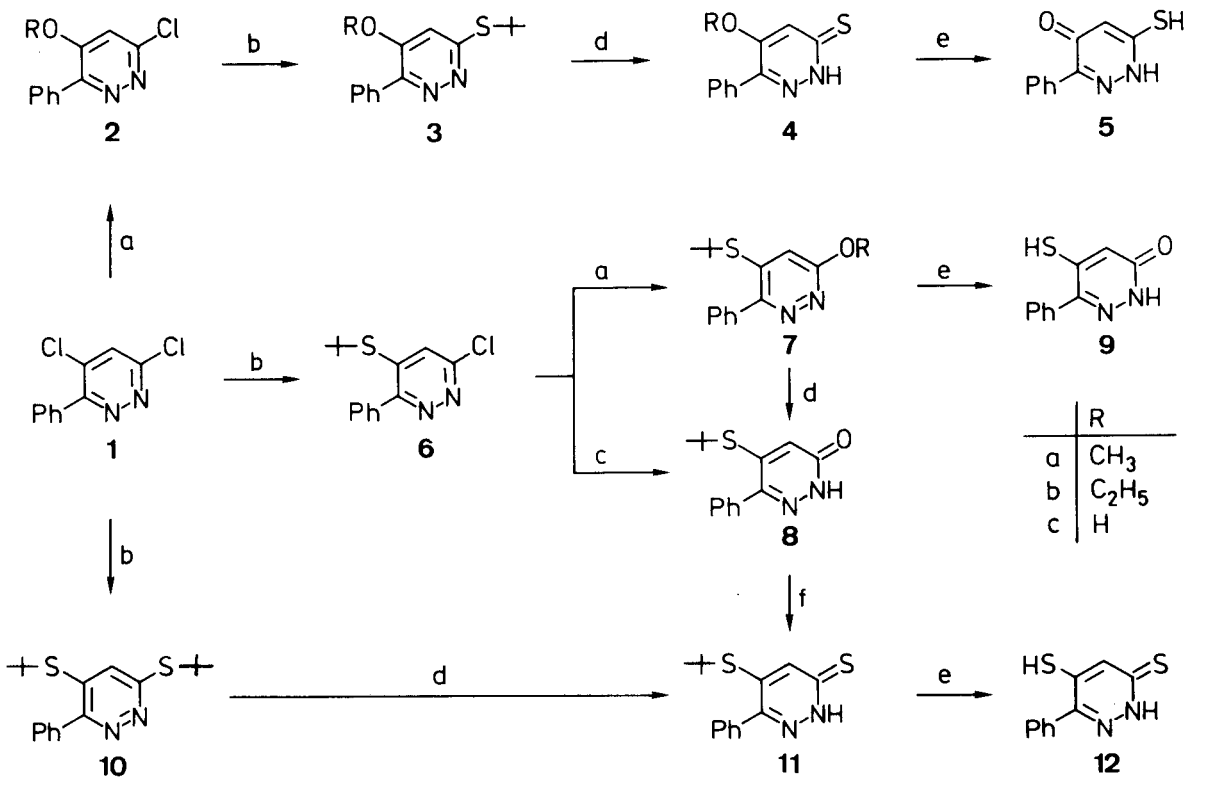
Cleavage of the alkyl ether as well as the *t*-butyl thioether bond in the compounds shown in Scheme 1, could be carried out regioselectively, due to different reactivity. Thus a *t*-butylthio group at position 3 can be cleaved with concentrated hydrochloric acid, whereas a substitutent at position 5 is cleaved only under forced conditions, by Lewis acids such as aluminium trichloride.

With the mixed alkyl ether and *t*-butylthio ethers the reactions also were regioselective as the same order of reactivity was found for the 3,5-di(*t*-butylthio)-6-phenylpyridazine **10**.

Compound **11** was prepared *via* two independent routes, first by reflux of compound **10** in concentrated hydrochloric acid, and secondly by treating 5-*t*-butylthio-6-phenylpyridazin-3(2*H*)-one **7** with phosphorus pentasulfide. The compounds obtained by both routes were identical. This observation confirms that the halogen at position 5 in 3,5-dichloro-6-phenylpyridazine is the most nucleofugic in the reaction with the 2-methyl-2-propanethiolate anion.

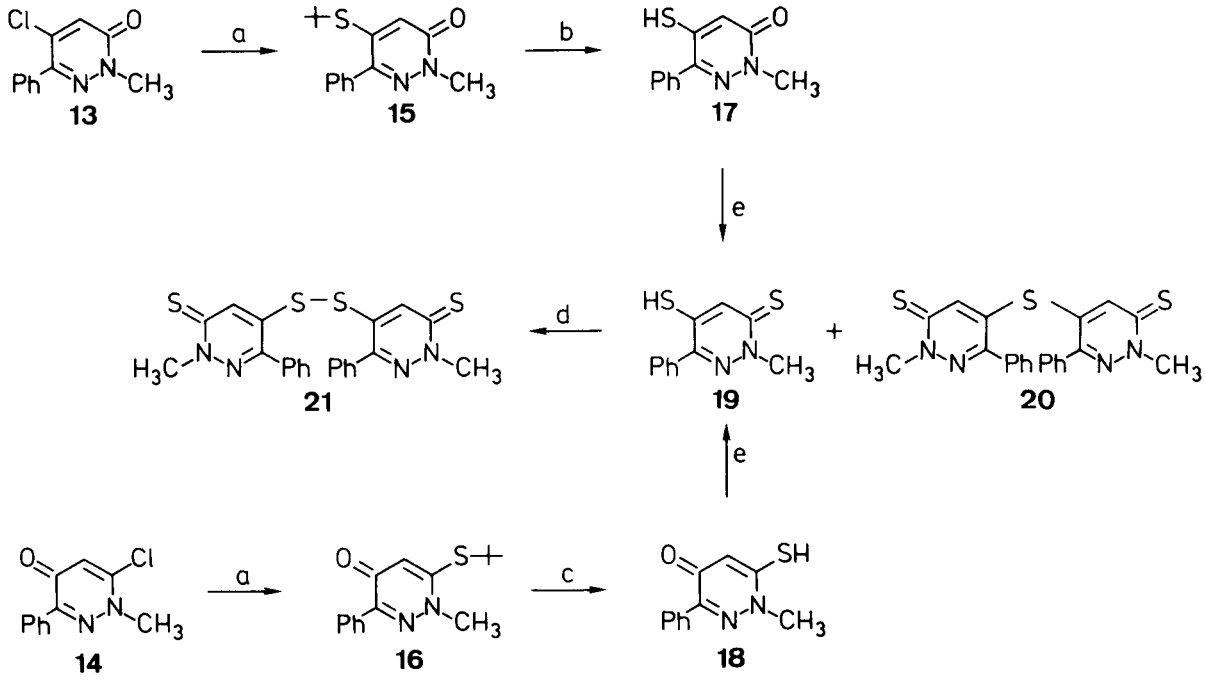
The nucleophilic reaction of the halogens with the 2-methyl-2-propanethiolate anion in the chloropyridazinones **13** and **14**, was in both cases performed as described for 3,5-dichloro-6-phenylpyridazine **1**.

Scheme 1



a: RONa, b: $(CH_3)_3CSNa$ in 2-propanol, c: NaOH in water/2-propanol, d: conc. HCl, e: $AlCl_3$ in toluene, f: P_2S_5 in toluene.

Scheme 2



a: $(CH_3)_3CSNa$ in 2-propanol, b: $AlCl_3$ in toluene, c: conc. HCl, e: P_2S_5 in toluene.

Elimination of the *t*-butyl moiety in the resulting compounds **15** and **16** followed the reactivity and selectivity described above. Thus the *t*-butylthio ether group in the 3-*t*-butylthio-2-methylphenylpyridazin-5-one **16**, on reflux in concentrated hydrochloric acid yielded 3-mercapto-2-methyl-6-phenylpyridazine-5-one **18**, whereas the *t*-butylthio ether moiety in the 5-*t*-butylthio-2-methyl-6-phenylpyridazine-3(2H)-one **15** reacted under more vigorous conditions with aluminum trichloride in refluxing toluene yielding 5-mercapto-2-methyl-6-phenylpyridazin-3(2*H*)-one **17**.

Compound **17** and **18** gave with phosphorus pentasulfide the same mixtures of products, namely the expected 5-mercapto-2-methyl-6-phenylpyridazine-3(2*H*)-thione **19** along with a minor side product identified as bis-(2-methyl-6-phenyl-2,3-dihydro-3-thioxopyridazin-5-yl) sulfide **20**. The yield of compound **20** was dependent upon reaction time as the dimer results from a secondary reaction, thus 5-mercapto-3-methyl-6-phenylpyridazine-3(2*H*)-thione **19** on reaction with phosphorus-pentasulfide directly yielded the dimeric product **20** in fair yield.

Compound **20** was assigned the structure depicted in Scheme 2, the phenyl protons in ^{1}H nmr spectrum have the same chemical shift, and appear as a singlet. In general a splitting of the phenyl protons are only seen in the ^{1}H nmr spectrum when there is an oxo or thioxo group *ortho* to the 6-phenyl group, because of interaction between the *ortho*-protons and the oxo or thioxo moiety. This splitting is not seen when position-5 is substituted with an alkyl ether or an alkyl thoiether group.

Compound **19** is readily oxidized by air to the disulfide **21**. The bis-5,5'-dithio structure of the resulting product **21** is assigned on the basis of the singlet seen in the ^{1}H nmr spectrum for the protons in the phenyl group as described above.

Conclusion.

Structures of the compounds described here were all in agreement with synthesis, analytical and spectroscopic values. The yields are generally fair to high, and the method is found to introduce sulfur selectively into the 3- or 5-positions of the 6-phenylpyridazine ring system. This method may therefore be expected to be of general value in related heterocyclic systems.

EXPERIMENTAL

The melting points were determined in open capillary tubes on a Gallenkamp melting point apparatus, MFB 595. The ir spectra were recorded on a Perkin-Elmer 298 spectrophotometer using samples in potassium bromide disks. The nmr spectra were recorded with a Varian EM-360 spectrometer at 60 MHz with TMS as an internal standard.

3-*t*-Butylthio-5-methoxy-6-phenylpyridazine (**3a**).

Sodium cuttings (1.15 g, 0.05 mole) were added to 75 ml of 2-propanol. The sodium was dissolved under reflux whereupon *t*-butylmercaptan (6 ml, 0.055 mole) was slowly added. After cooling to room temperature the solution became semisolid. Then 3-chloro-5-methoxy-6-phenylpyridazine **2a** [8], (11 g, 0.05 mole) was added and the reaction mixture heated at reflux for 1 hour. After cooling the mixture was poured into 200 ml of ice-water and made strongly alkaline with 50 ml of sodium hydroxide (1*M*). After extraction with dichloromethane (3 × 50 ml), drying (magnesium sulfate) and concentration *in vacuo* the title compound crystallized upon trituration with petroleum ether. Recrystallization yielded **3a** (20%) as white crystals, mp 90-93° (petroleum ether); ir: 1410 s, 1570 s cm^{-1}; nmr (deuteriochloroform): δ 1.66 (s, 9, *t*-butyl), 3.76 (s, 3, CH_3), 6.76 (s, 1, pyr H), 7.3-7.5 (m, 3, m ArH), 7.8-8.0 (m, 2, ArH).

Anal. Calcd. for $C_{15}H_{18}N_2OS$: C, 65.66; H, 6.61; N, 10.21; S, 11.69. Found: C, 65.88; H, 6.73; N, 10.22; S, 11.20.

From the aqueous phase 5-hydroxy-3-chloro-6-phenylpyridazine **2c**, was isolated after acidification with concentrated hydrochloric acid, yield 32%, mp 214-216° (ethanol).

3-*t*-Butylthio-5-ethoxy-6-phenylpyridazine (**3b**).

The sodium 2-methyl-2-propanethiolate was prepared as described above, from sodium (5 g, 0.22 mole) and *t*-butylmercaptan (23 ml, 0.20 mole) in 200 ml of 2-propanol. To this salt was added 3-chloro-5-ethoxy-6-phenylpyridazine **2b** [8] (42 g, 0.20 mole) and the temperature slowly raised to reflux, and kept at this temperature for 1 hour. After cooling the reaction mixture was poured into 400 ml of icewater. The precipitate was filtered, washed with water and recrystallized. The yield of **3b** was 73%, mp 88-90° (petroleum ether); ir: 1450 s, 1570 s cm^{-1}; nmr (deuteriochloroform): δ 1.66 (s, 9 *t*-butyl), 1.33-1.60 (t, 3, CH_3, J = 7 Hz), 3.90-4.27 (q, 2, CH_2, J = 7 Hz), 6.80 (s, 1, pyr H), 7.3-7.5 (m, 3, ArH), 7.8-8.0 (m, 2, ArH).

Anal. Calcd. for $C_{16}H_{20}N_2OS$: C, 66.83; H, 6.99; N, 9.71; S, 11.12. Found: C, 66.98; H, 6.72; N, 9.73; S, 10.89.

5-Methoxy-6-phenylpyridazine-3(2*H*)-thione (**4a**).

3-*t*-Butylthio-5-methoxy-6-phenylpyridazine **3a** (1 g, 3.64 mmoles), was heated at reflux in 30 ml of concentrated hydrochloric acid for 1 hour. The title compound separated on cooling. It was filtered, washed with water and recrystallized. The yield of **4a** was 82%, mp 175-177° (ethanol); ir: 3140 s, cm^{-1}; nmr: δ 3.73 (s, 3 CH_3), 7.04 (s, 1, pyr H); 7.15-7.6 (m, 5, ArH), 14.2 (s, broad, 1, NH).

Anal. Calcd. for $C_{11}H_{10}N_2OS$: C, 60.53; H, 4.62; N, 12.83; S, 14.66. Found: C, 60.66; H, 4.65; N, 12.84; S, 14.43.

5-Ethoxy-6-phenylpyridazine-3(2*H*)-thione (**4b**).

3-*t*-Butylthio-5-ethoxy-6-phenylpyridazine **3b** (41 g, 0.14 mole) was heated at reflux in 200 ml of concentrated hydrochloric acid for 1 hour. After cooling the reaction mixture was poured on 300 ml of ice-water. The title compound which separated, was filtered, washed with water, and recrystallized. The yield of **4b** was 86%, mp 218-220° (ethanol); ir: 3160 s, cm^{-1}; nmr (hexadeuteriodimethylsulfoxide): δ 1.66 (t, 3, CH_3, J = 7 Hz), 4.25 (q, 2, CH_2, J = 7 Hz), 7.13 (s, 1, pyr H), 7.2-7.8 (m, 5, ArH), 14.30 (s, broad, 1, NH).

Anal. Calcd. for $C_{12}H_{12}N_2OS$: C, 62.04; H, 5.21; N, 12.06; S, 13.80. Found: C, 62.27; H, 5.15; N, 11.96; S, 13.51.

5-Hydroxy-6-phenylpyridazine-3(2*H*)-thione (**5**).

Method A.

To a solution of 3-*t*-butylthio-5-ethoxy-6-phenylpyridazine **3b**, (7.2 g, 0.025 mole) in 50 ml of dry toluene, aluminium trichloride (10 g, 0.075 mole) was added. The reaction mixture was heated at reflux for 1 hour. After cooling the mixture was poured into 100 ml ice-water, whereupon 10 ml of 1*N* hydrochloric acid solution was added and the mixture was stirred vigorously for 1 hour. The title compound which separated was filtered and recrystallized.

Method B.

To a solution of 5-ethoxy-6-phenylpyridazine-3(2*H*)-thione **4b**, (5.75 g, 0.25 mole) in 75 ml of dry toluene, aluminium trichloride, (10 g, 0.075

mole) was added. The reaction mixture was heated at reflux for 1 hour. The compound was isolated and purified as described above. The yield was 85%, (A); and 70% (B); mp 261-263° (acetic acid); ir: 1600 s 3200 NH, cm^{-1}; nmr (hexadeuteriodimethyl sulfoxide): δ 3.66 (s, broad, 1, SH), 7.10 (s, 1, pyr H), 7.3-7.5 (m, 3, ArH), 7.5-7.9 (m, 2, ArH), 14.3 (s, broad, 1, NH).

Anal. Calcd. for $C_{10}H_8N_2OS$: C, 58.81; H, 3.95; N, 13.71; S, 15.70. Found: C, 58.91; H, 3.98; N, 13.56; S, 15.71.

5-*t*-Butylthio-3-chloro-6-phenylpyridazine (**6**).

Sodium 2-methyl-2-propanethiolate was prepared as described above, from sodium , (5 g, 0.22 mole) and *t*-butylmercaptane (23 ml, 0.20 mole) in 200 ml of 2-propanol. The salt was added to a solution of 3,5-dichloro-6-phenylpyridazine **1**, (44.8 g, 0.20 mole) in 100 ml of 2-propanol, at 0° with stirring during 0.5 hour. After addition the reaction mixture was kept at 0° for 0.5 hour, and then slowly heated to room temperature, and kept at this temperature for 0.5 hour. The reaction mixture was poured into 500 ml of ice-water, and the precipitate was filtered and recrystallized. The yield of **6** was 74%, mp 101-102° (petroleum ether 50-60°); ir: 1530 s, cm^{-1}; nmr (deuteriochloroform): δ 1.43 (s, 9, *t*-butyl), 7.56 (s, 1, pyr H), 7.30-7.66 (m, 5, ArH).

Anal. Calcd. for $C_{14}H_{15}ClN_2S$: C, 60.33; H, 5.42; N, 10.05; S, 11.50. Found: C, 60.51; H, 5.62; N, 10.01; S, 11.31.

5-*t*-Butylthio-3-methoxy-6-phenylpyridazine (**7a**).

Sodium (1.0 g, 0.044 mole) was dissolved in 50 ml of methanol. To this solution was added 5-*t*-butylthio-3-chloro-6-phenylpyridazine **6**, (6.75 g, 0.024 mole) and the reaction mixture heated at reflux for 0.5 hours. After cooling the solution was filtered and evaporated *in vacuo*. The resulting oil was recrystallized. The yield of **7a** was 49%, mp 79-80° (pentane); ir: 1530 s cm^{-1}; nmr (deuteriochloroform): δ 1.33 (s, 9, *t*-butyl), 4.17 (s, 3, CH_3), 7.13 (s, 1, pyr H), 7.2-7.6 (m, 5, ArH).

Anal. Calcd. for $C_{15}H_{18}N_2OS$: C, 65.66; H, 6.61; N, 10.21; S, 11.69. Found: C, 65.78; H, 6.72; N, 10.32; S, 11.43.

5-*t*-Butylthio-3-ethoxy-6-phenylpyridazine (**7b**).

Sodium (2 g, 0.08 mole) was dissolved in 50 ml of ethanol. To this solution was added 5-*t*-butylthio-3-chloro-6-phenylpyridazine **6** (7 g, 0.023 mole), and the reaction mixture was heated at reflux for 0.5 hour. After cooling the reaction mixture was poured into ice-water (100 ml), and the title separated. It was filtered and recrystallized. The yield of **7b** was 77%, mp 116-117° (petroleum ether); ir: 1420 s, 1560 s cm^{-1}; nmr (deuteriochloroform): δ 1.33 (s, 9, *t*-butyl), 1.33-1.60 (t, 3, CH_3, J = 7 Hz), 4.4-4.76 (q, 2, CH_3, J = 7 Hz), 7.10 (s, 1, pyr H), 7.3-7.7 (m, 5, ArH).

Anal. Calcd. for $C_{16}H_{20}N_2OS$: C, 66.83; H, 6.99; N, 9.71; S, 11.12. Found: C, 66.72; H, 7.10; N, 9.89; S, 10.65.

5-*t*-Butylthio-6-phenylpyridazin-3(2*H*)-one (**8**).

Method A.

5-*t*-Butylthio-3-chloro-6-phenylpyridazine **6**, (7 g, 0.025 mole) was dissolved in 30 ml of 2-propanol. To this solution was added 5 g of sodium hydroxide dissolved in 10 ml water and the reaction mixture heated at reflux for 24 hours. After cooling it was poured into ice-water (200 ml), and filtered. The filtrate was acidified with concentrated hydrochloric acid, and the title compound separated. It was filtered, dried and recrystallized.

Method B.

5-*t*-Butylthio-3-methoxy-6-phenylpyridazine **7a**, (1.5 g, 5.4 mmoles) was heated at reflux in concentrated hydrochloric acid for 1.5 hours. After cooling the title compound separated. It was filtered, washed with water, dried and recrystallized.

The yield of **8** was 42% by method A and 53% by method B, mp 211-213° (toluene); ir: 1665 g, 3200 NH cm^{-1}; nmr (hexadeuteriodimethyl sulfoxide): δ 1.33 (s, 9, *t*-butyl), 6.92 (s, 1, pyr H), 7.47 (s, 5, ArH), 13.0 (s, broad, 1, NH).

Anal. Calcd. for $C_{14}H_{16}N_2OS$: C, 64.58; H, 6.19; N, 10.76. Found: C, 64.86; H, 6.43; N, 10.69.

5-Mercapto-6-phenylpyridazin-3(2*H*)-one (**9**).

To a solution of 5-*t*-butylthio-3-ethoxy-6-phenylpyridazine **7b** (7.2 g, 0.025 mole) in 50 ml of dry toluene was added aluminium trichloride (10 g, 0.075 mole). The reaction mixture was heated at reflux for 1 hour. The compound was purified according to the procedure described for compound **5**. The yield of **9** was 61% mp 298-304° (acetic acid); ir: 1675, 2540, 3070 cm^{-1}; nmr (hexadeuteriodimethyl sulfoxide): δ 3.9 (s, broad, 1, SH), 7.23 (s, 1, pyr H), 7.40 (s, 5, ArH), 13.20 (s, broad, 1, NH).

Anal. Calcd. for $C_{10}H_8N_2OS$: C, 58.81; H, 3.95; N, 13.71; S, 15.70. Found: C, 58.67; H, 3.98; N, 13.63; S, 15.42.

3,5-Di-*t*-butylthio-6-phenylpyridazine (**10**).

Sodium 2-methyl-2-propanethiolate was prepared as described above, from sodium (5 g, 0.22 mole) and *t*-butylmercaptan (23 ml, 0.205 mole) in 100 ml of 2-propanol. The sodium salt was added in small portions to a stirred solution of 3,5-dichloro-6-phenylpyridazine **1**, (22 4 g, 0.10 mole) in 100 ml of 2-propanol at 0°. After addition the reaction mixture was stirred at 0° for 0.5 hours, and then heated at reflux for 1 hour. After cooling the reaction mixture was poured into ice-water (500 ml). The precipitate was filtered, washed with water, dried and recrystallized. The yield of **10** was 76%, mp 104-105° (2-propanol); ir: 1540 cm^{-1}; nmr (deuteriochloroform): δ 1.30 (s, 9, *t*-butyl), 1.66 (s, 9, *t*-butyl), 7.43 (s, 1, pyr H), 7.2-7.8 (m, 5, ArH).

Anal. Calcd. for $C_{18}H_{24}N_2S_2$: C, 65.02; H, 7.27; N, 8.42; S, 19.28. Found: C, 65.34; H, 7.32; N, 8.30; S, 18.88.

5-*t*-Butylthio-6-phenylpyridazine-3(2*H*)-thione (**11**).

Method A.

3,5-Di-*t*-butylthio-6-phenylpyridazine **10**, (3 g) was heated at reflux in concentrated hydrochloric acid, 50 ml, for 0.5 hour. After cooling the precipitate was filtered, washed with water, dried and recrystallized.

Method B.

To a suspension of 5-*t*-butylthio-6-phenylpyridazin-3(2*H*)-one **8**, (0.5 g, 1.9 mmoles) in 10 ml dry toluene was added phosphorus pentasulfide (1.5 g). The reaction mixture was heated at reflux for 0.5 hour. After cooling it was evaporated *in vacuo*. The residue obtained was recrystallized. The yield of **11** was 76% (A) and 72% (B) mp 248-250° (ethanol); ir: 3140 cm^{-1}; nmr (hexadeuteriodimethyl sulfoxide): δ 1.37 (s, 9, *t*-butyl), 7.40 (s, 5, ArH), 7.56 (s, 1, pyr H), 14.50 (s, broad, 1, NH).

Anal. Calcd. for $C_{10}H_8N_2S_2$: C, 60.82; H, 5.83; N, 10.13; S, 23.20. Found: C, 60.55; H, 5.65; N, 10.22; S, 23.32.

5-Mercapto-6-phenylpyridazine-3(2*H*)-thione (**12**).

To a solution of 3,5-di-*t*-butylthio-6-phenylpyridazine **10** (3.5 g, 0.01 mole) in dry toluene, 50 ml, aluminium trichloride (4.5 g, 0.03 mole) was added, and the reaction mixture heated at reflux for 0.5 hour. The compound was purified according to the procedure described for compound **5**. The yield of **12** was 77%, mp 207-208° (acetic acid); ir: 2400, 3300 cm^{-1}; nmr (hexadeuteriodimethylsulfoxide): δ 7.53 (s, 5, ArH), 7.63 (s, 1, pyr H), 14.66 (s, broad, 1, NH).

Anal. Calcd. for $C_{10}H_8N_2S_2$: C, 54.52; H, 3.66; N, 12.74; S, 29.11. Found: C, 54.53; H, 3.59; N, 12.65; S, 28.91.

5-*t*-Butylthio-2-methyl-6-phenylpyridazin-3(2*H*)-one (**15**).

Sodium 2-methyl-2-propanethiolate was prepared as described above from sodium (2.5 g, 0.11 mole) and *t*-butylmercaptan (11.5 ml, 0.105 mole) in 100 ml of 2-propanol. To this salt 5-chloro-2-methyl-6-phenylpyridazin-3(2*H*)-one, **13** [8], (22.5 g 0.1 moles) was added with stirring and cooling to 0°. The reaction mixture was heated at reflux for 0.5 hour, and after cooling to room temperature it was poured into 300 ml of ice-water. The precipitate was filtered and recrystallized. The yield of **15** was 68%, mp 109-110° (cyclohexane); ir: 1655 cm^{-1}; nmr (deuteriochloroform): δ 1.43 (s, 9, *t*-butyl), 3.76 (s, 3, CH_3), 7.02 (s, 1, pyr H), 7.40 (s, 5, ArH).

Anal. Calcd. for $C_{15}H_{18}N_2OS$: C, 65.66; H, 6.61; N, 10.21; S, 11.69. Found: C, 65.82; H, 6.61; N, 10.20; S, 11.56.

3-*t*-Butylthio-2-methyl-6-phenyl-5*H*-pyridazin-5-one (**16**).

The same procedure as described for compound **15** was used, starting from 3-chloro-2-methyl-6-phenylpyridazine-5-one, **14** [10], (22.59 g, 0.1 mole). The yield of **16** was 86%, mp 103-104° (cyclohexane/petroleum ether); ir: 1610 cm^{-1}; nmr (deuteriochloroform): δ 1.43 (s, 9, *t*-butyl), 4.05 (s, 3, CH_3), 6.80 (s, 1, pyr H), 7.2-7.5 (m, 3, ArH), 8.0-8.2 (m, 2, ArH).

Anal. Calcd. for $C_{15}H_{18}N_2OS$: C, 65.66; H, 6.61; N, 10.21; S, 11.69. Found: C, 65.69; H, 6.64; N, 10.16; S, 11.50.

5-Mercapto-2-methyl-6-phenylpyridazin-3(2*H*)-one (**17**).

To a solution of 5-*t*-butylthio-2-methyl-6-phenylpyridazin-3(2*H*)-one, **15**, (11 g, 0.04 mole) in 75 ml of dry toluene aluminium trichloride (12 g, 0.09 mole) was added. The reaction mixture was heated at reflux for 0.5 hour, and after cooling to room temperature it was poured into 150 ml ice-water. Hydrochloric acid (10 ml, 1*M* was added to the heterohomogeneous solution and stirred for 1 hour and the precipitate was filtered. A small amount of the title compound was isolated from the toluene phase by extraction with sodium hydroxide solution (2 × 25 ml of 1 *M*). Upon acidification of these extracts the title compound precipitated. The combined filtrates were dried and recrystallized. The yield of **17** was 98%, mp 152-154° (toluene); ir: 1630, 1655, 2430 cm^{-1}; nmr (hexadeuteriodimethyl sulfoxide): δ 3.70 (s, 3, CH_3), 7.00 (s, 1, pyr H), 7.43 (s, 5, ArH).

Anal. Calcd. for $C_{11}H_{10}N_2OS$: C, 60.53; H, 4.62; N, 12.83; S, 14.66. found: C, 60.20; H, 4.76; N, 12.71; S, 14.35.

5-Hydroxy-2-methyl-6-phenylpyridazine-3(2*H*)-thione (**18**).

3-*t*-Butylthio-2-methyl-6-phenyl-5*H*-pyridazin-5-one, **16**, (11 g, 0.04 mole) was boiled in 100 ml of concentrated hydrochloric acid solution for 1.5 hours. After cooling to room temperature the precipitate was filtered, washed with water and recrystallized. The yield of **18** was 82%, mp 239-240° (ethanol); ir: 1605 cm^{-1}; nmr (hexadeuteriodimethyl sulfoxide): δ 3.95 (s, 3, CH_3), 7.20 (d, 1, pyr H), 7.3-7.5 (m, 3, ArH), 7.4-7.7 (m, 2, ArH).

Anal. Calcd. for $C_{11}H_{10}N_2OS$: C, 60.53; H, 4.62; N, 12.83; S, 14.66. Found: C, 60.66; H, 4.69; N, 12.76; S, 14.50.

5-Mercapto-2-methyl-6-phenylpyridazine-3(2*H*)-thione (**19**).

Method A.

Suspension of 5-hydroxy-2-methyl-6-phenylpyridazine-3(2*H*)-thione **17** (2 g, 0.009 mole), in 50 ml of dry toluene was heated at reflux. At this temperature phosphorus pentasulfide (3 g) was added to the suspension during 5 minutes. After addition the reaction mixture was heated at reflux for 20 minutes, then cooled to room temperature and 75 ml aqueous sodium hydroxide (2*N*) was added with vigorous stirring. The heterogeneous solution was filtered and the two phases separated. The aqueous phase was acidified with concentrated hydrochloric acid. The precipitate was filtered, dried and recrystallized.

Method B.

In precisely the same manner the reaction was carried out starting 5-mercapto-2-methyl-6-phenylpyridazine-3(2*H*)-one, **18** (4 g, 0.018 mole), in 75 ml of dry toluene and phosphorus pentasulfide (6 g). The yield of **19** was 55% (A) and 53% (B), mp 134-136° (ethanol); ir: 2450 cm^{-1}; nmr (hexadeuteriodimethyl sulfoxide): δ 4.00 (s, 3, CH_3), 7.50 (s, 5, ArH), 7.93 (s, 1, pyr H).

Anal. Calcd. for $C_{11}H_{10}N_2S_2$: C, 56.37; H, 4.30; N, 11.95; S, 27.36. Found: C, 56.52; H, 4.23; N, 11.90; S, 27.38.

From the toluene extract a small amount of compound **20** could be isolated upon evaporation *in vacuo*, and recrystallization of the residue. The yield was 9% (A), and 5% (B).

Bis-(2-methyl-6-phenyl-2,3-dihydro-3-thioxypyridazin-5-yl) Sulfide, **20**.

To a solution of 5-mercapto-2-methyl-6-phenylpyridazine-3(2*H*)-thione, **19** (0.3 g, 1 mmole) in 20 ml of toluene, phosphorus pentasulfide (1 g) was added and the reaction mixture was heated at reflux for 4 hours. The solvent was evaporated *in vacuo*, and 30 ml ethanol was added to the residue. The mixture was heated to reflux and filtered hot. Upon cooling the title compound precipitated. It was filtered and recrystallized. The yield of **20** was 65%, mp 198-200° (acetic acid); nmr (hexadeuteriodimethyl sulfoxide): δ 4.03 (s, 6, CH_3), 7.33 (s, 10, ArH), 7.50 (s, 2, pyr H).

Anal. Calcd. for $C_{22}H_{18}N_4S_3$: C, 60.80; H, 4.17; N, 12.89; S, 22.13. Found: C, 60.96; H, 4.11; N, 12.86; S, 21.83.

Bis-(2-methyl-6-phenyl-2,3-dihydro-3-thioxopyridazin-5-yl) Disulfide (**21**).

A solution of 5-mercapto-2-methyl-6-phenylpyridazine-3(2*H*)-thione, **19**, in 30 ml of chloroform was stirred for 3 days at room temperature. The reaction mixture was evaporated *in vacuo*, and the residue recrystallized. The yield of **21** was 60%, mp 164-164° (acetic acid); nmr (hexadeutiodimethyl sulfoxide): δ 4.17 (s, 6, CH_3), 7.53 (s, 10, ArH), 7.73 (s, 2, pyr H).

Anal. Calcd. for $C_{22}H_{18}N_4S_4$: C, 56.62; H, 3.89; N, 12.01; S, 27.48. Found: C, 56.40; H, 3.65; N, 11.86; S, 27.71.

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