Synthesis of Analogues of the 2,3,6,-Triazaphenothiazine Ring System (1)

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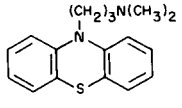
Received August 31, 1982

Treatment of 2,3-dichloroquinoxalines with 2-amino-6-picoline-3-thiol gave a mixture of 2,3-bis(2-amino-6-picolinyl-3-thio)quinoxalines (**16**, R = H, Cl) and 2,3-bis (*N,N*-dimethylamino)quinoxalines (**15**, R = H, Cl) separated by fractional crystallization. A similar reaction of 3-amino-6-methoxypyridine-2(1*H*)-thione (**9**) with 4,5-dichloropyridazin-3(2*H*)-one (**21**) gave 4-chloro-5-(3-amino-6-methoxypyridyl-2-thio)pyridazin-3(2*H*)-one (**22**). Concentrated hydrochloric acid-catalysed cyclization of **22** gave the non-rearranged 7-methoxy-2,3,6-triazaphenothiazin-1(2*H*)-one. The action of compound **22** in refluxing glacial acetic acid gave, on the other hand, 7-methoxy-2,3,6-triazaphenothiazin-4(3*H*)-one *via* a Smiles rearrangement. These cyclized compounds are the first known derivatives of the new 2,3,6-triazaphenothiazine ring system.

J. Heterocyclic Chem., **20**, 199 (1983).

Since the discovery of the antipsychotic properties of chlorpromazine (**1**) nearly three decades ago (4), several other useful neuroleptics have been developed. Although many of them are the conventional side chain derivatives, a good number, however, have no structural relationship with phenothiazine or chlorpromazine. Among the compounds in the latter class are Droperidol (**2**) (5), Oxypertine (**3**) (6) and Sulpiride (**4**) (7).



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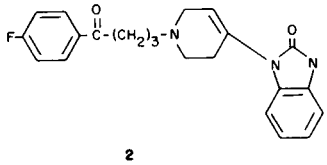

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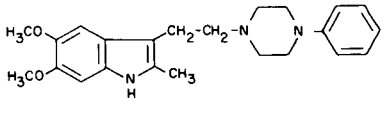

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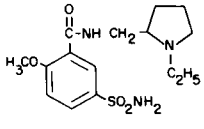

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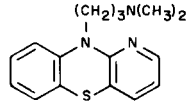
While these newer drugs are reasonably potent, the general impression from medical practitioners is that phenothiazine-based compounds are more suitable for the treatment of acute psychoses, their side effects not withstanding. Hift, Quandt and their groups independently showed that prothipendyl (**5**), the 1-azaphenothiazine analog of promazine could even be a superior drug (8) to chlorpromazine in treating psychiatric conditions. It also has fewer side effects (9) than promazine or chlorpromazine. The latter report led to an upsurge in the synthesis of aza-analogues of phenothiazine and thus attention was focused once again on azaphenothiazines (10-11). So far,



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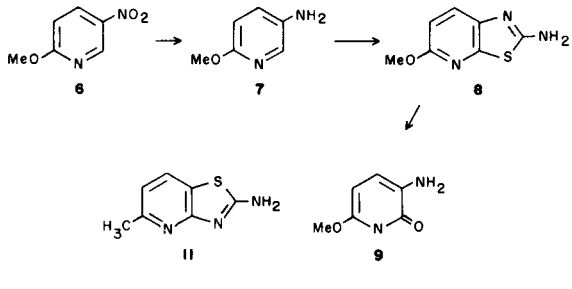
all of the four monoaza analogs (10) of phenothiazine have been synthesized. Out of fifteen, twenty-four and thirty-five possible structural isomers in the more complex diaza-, triaza- and tetraazaphenothiazine series, only ten (10-14), four (11,15-16) and seven (17-19) isomeric ring systems, respectively, have now been synthesized successfully. The "open" systems (20-21) and the analogs (22) in which sulfur was replaced with oxygen were also prepared. These "open" and "closed" azaphenothiazines and phenoxazines were found to have CNS depressant activities (21,24). We have now successfully synthesized new variations in the azaphenothiazine structure.

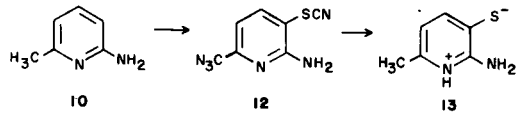
The starting compound, 2-methoxy-5-nitropyridine (**6**) was reduced to the 5-amino derivative **7** with hydrogen and 10% Palladium on carbon or with the newly developed iron calcium chloride reagent (15) followed by treatment with sodium thiocyanate and bromine in glacial acetic acid. The resulting 2-amino-5-methoxythiazolo-

Scheme I



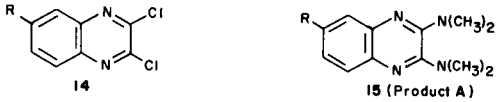
[5,4-*b*]pyridine (**8**) was saponified and acidified to afford 3-amino-6-methoxypyridine-2(1*H*)-thione (**9**) in excellent yields (Scheme 1). A similar reaction with 2-amino-6-picol-

ine (**10**) did not yield the thiazolo[4,5-*b*]pyridine (**11**). In its place a fair yield of 2-amino-3-thiocyanato-6-picoline (**12**) was obtained. Hydrolysis of **12** gave the 3-thiol as the zwitterionic salt **13**.



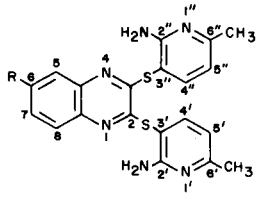
10 12 13

Treatment of compounds **13** with 2,3-dichloroquinoxaline (**14**, R = H) in refluxing alkaline aqueous DMSO or DMF for 15 hours gave two products **A** and **B** in 18% and 77% yields, respectively. The low melting compounds **A** (mp 63.5-64.5°) was shown by analysis, mass spectrometry [M^+ at m/e 216 (32%)] and nmr spectroscopy (δ 3.03, s, 2-NMe_2, 3-NMe_2; δ 7.50, m, four aromatic protons) to be 2,3-bis(*N,N*-dimethylamino)quinoxaline (**15**, R = H).



14 15 (Product A)

While previous reactions of 2,3-dichloroquinoxaline with *o*-aminoheterocyclic thiols (25) gave the corresponding azaphenothiazines, the main product **B** obtained in this case (mp >300°) does not have the usual characteristics of azaphenothiazines. Analysis and nmr spectroscopy are in agreement with structure **16**, R = H.

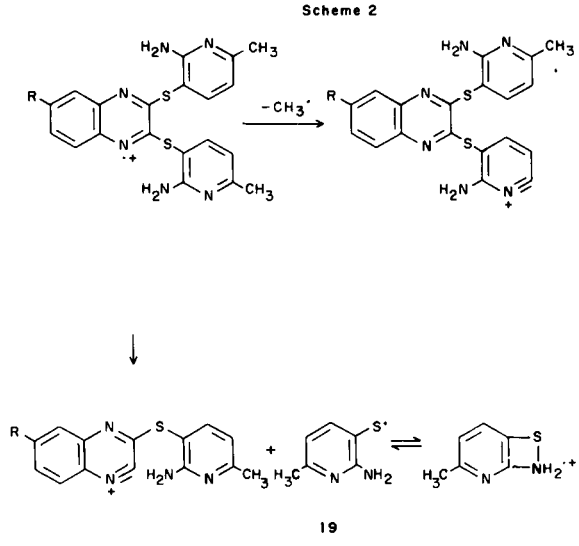


16 (Product B)

If 2,3,6-trichloroquinoxaline (**14**, R = Cl) is used in these reactions in the place of **14**, R = H, 6-chloro-2,3-di(*N,N*-dimethylamino)quinoxaline (**15**, R = Cl, mp 78-79°) and 6-chloro-2,3-bis(2-amino-6-picolinyl-3-thio)quinoxaline (**16**, R = Cl, mp 256.5-257.5°) were obtained as products **A** and **B** in 24% and 71% yields, respectively. When the reactions were carried out in anhydrous DMSO or DMF in the presence of potassium hydroxide only compounds **16** were isolated in both cases in poor yields (12%) (26).

Confirmatory evidence for the assigned structures **16**, R = H, Cl was obtained by mass spectroscopy as shown in Scheme 2. Loss of a methyl radical by the parent ions led

Scheme 2



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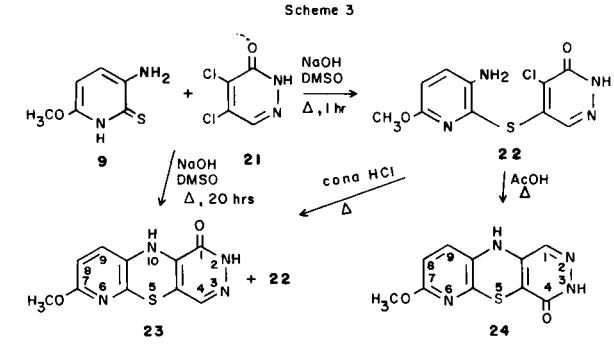
to the prominent peaks **17**, R = H, Cl (27). The base peaks in both spectra were obtained by the cleavage of the one C-S bond in the parent ion leading to the pyridylquinoxalinyl sulfide ion **18** and the aminopyridyl mercaptide radical **19** which is probably in equilibrium with the bicyclic radical ion **20**.

However, when 3-amino-6-methoxypyridine-2(1*H*)-thione (**9**) was treated with 4,5-dichloropyridazin-6(1*H*)-one (**21**) in aqueous alkaline dimethyl sulfoxide (DMSO) for one hour, the diaryl sulfide **22** was obtained in good yield. By extending the reaction time to 20 hours, a mixture of **22** and a red crystalline product was obtained. These compounds were separated satisfactorily by fractional crystallization from aqueous ethanol. Analysis, infrared, mass and nmr spectroscopy of the latter product are in agreement with structure **23** or **24**.

Scheme 3

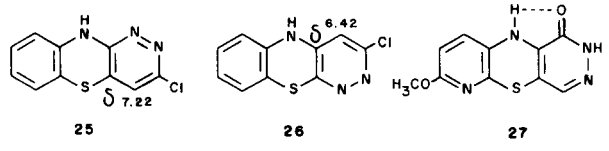


9 21 22 23 24

In order to decide on the exact structure, the precursor **22** was treated with concentrated hydrochloric acid, a reagent which induces cyclization without rearrangement (28,29). Refluxing **12** with concentrated hydrochloric acid gave a product identical with compound **23**, the non-rearranged structure. However, when compound **22** was refluxed for 16 hours in glacial acetic acid, the isomeric

cyclized structure **24** was obtained after workup. Compound **24** is an orange crystalline material melting above 300°. Microanalysis and spectroscopy are in agreement with the assigned rearranged structure **24** (Scheme 3).

On comparing the spectra of compounds **23** and **24**, the C-1 proton of structure **24** appears more shielded (absorption at δ 7.25) than the corresponding C-4 proton of the structure **23** (absorbs at δ 7.82). This observation is due to the greater electron releasing influence of the 10-NH group in **24** than in **23**. This interpretation is in agreement with the observation of Yoneda (28) in 3-chloro-1,2-diaza- (**25**) and 2-chloro-3,4-diazaphenothiazines (**26**).



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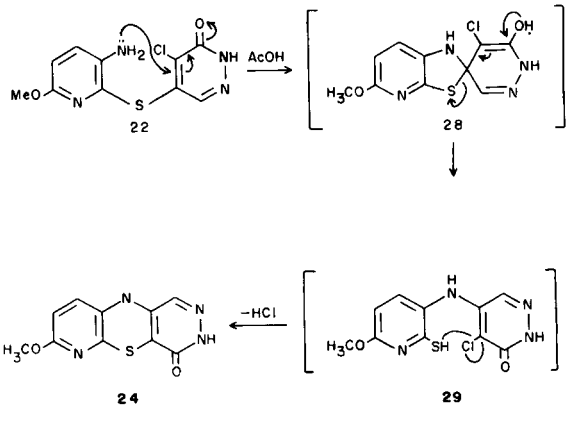
Because of the proximity of the 10-NH proton to the carbonyl oxygen in compound **23**, a stable 5-membered ring chelate could be formed through strong NHO hydrogen bonding (structure **27**). Evidence for this chelation is provided by the nmr spectrum in which the 10-NH proton appeared as a very broad singlet compared to a less broad 10-NH absorption in structure **24**. This observation is again in support of the assigned structures. Furthermore, the action of acetic acid or dilute acids in general on suitably substituted diaryl sulfides is now known to induce a Smiles rearrangement (23,28) and cyclization to the appropriate phenothiazine ring system.

Scheme 4



22 28 24 29

The mechanism for the formation of 7-methoxy-2,3,6-triazaphenothiazin-4(3*H*)-one (**24**) is shown in Scheme 4. These compounds **23** and **24**, are isomeric derivatives of the new 2,3,6-triazaphenothiazine ring systems.

EXPERIMENTAL

Melting points were determined with a Thomas-Hoover melting point apparatus and are uncorrected. The ir spectra were recorded on a Perkin Elmer Model 337 grating infrared spectrophotometer using potassium bromide discs. The ^{1}H-nmr spectra were determined on a Varian EM-360 60 MHz spectrometer in the solvents indicated. Chemical shifts are reported in ppm from TMS used as an internal standard and are given in δ units. The letters b, s, d and m are used to indicate broad, singlet, doublet and multiplet, respectively. Mass spectra were recorded on a Hewlett Packard model 5980A mass spectrometer at 70eV. Elemental analyses were performed by MHW Laboratories, Phoenix, Arizona and Istituto Superiore de Sanita, Rome, Italy.

Iron-Calcium Chloride Reduction of 2-Methoxy-5-nitropyridine (**6**).

To an intimate mixture of 2-methoxy-5-nitropyridine (7.7 g, 50 mmoles) and 30 g of finely powdered iron was added 200 ml of 75% ethanol and 5 g of calcium chloride. The entire exothermic mixture was refluxed on a steam bath for 4 hours. The unreacted iron was filtered off. The filtrate was then treated with activated charcoal and filtered. The resulting dark red solution was concentrated to dryness *in vacuo*. Fractional distillation of the residue gave 5-amino-2-methoxypyridine (**7**) as a red liquid (5.96 g, 96%) n_D^{20} = 1.5729. The same product was also obtained in nearly the same yield by stannous chloride and concentrated hydrochloric acid reduction of 2-methoxy-5-nitropyridine (**6**) as was previously described (30). However, the iron-calcium chloride reduction was found to be more convenient and less hazardous.

2-Amino-5-methoxythiazolo[5,4-*b*]pyridine (**8**).

This compound was prepared as previously, described (28) except that the slurry was stirred after bromine addition at 0° for 4 hours and 0-20° for 3 hours and at room temperature for 15 hours. The orange residue was extracted three times with glacial acetic acid. The combined products gave a nearly quantitative yield of 2-amino-5-methoxythiazolo-[5,4-*b*]pyridine (**8**).

3-Amino-6-methoxypyridine-2(1*H*)-thione (**9**).

This product was obtained as described previously (30). In view of its instability upon long exposure to heat and light, it was prepared just before use in the following step.

2-Amino-3-thiocyanato-6-picoline (**12**).

This compound was prepared from 2-amino-6-picoline as reported earlier (30) except that the initial yield was very low. However, more product was collected from the near neutral solution on chilling to 0 to -5° for several days and by repeating the cooling process several times.

2-Amino-6-picoline-3-thiol (**13**).

The hydrolysis of 2-amino-3-thiocyanato-6-picoline (**12**) was accomplished by refluxing with sodium hydroxide (31) for 5 hours followed by acidification.

4,5-Dichloropyridazin-3(2*H*)-one (**21**).

This compound was prepared from mucochloric acid and semicarbazide hydrochloride by extensive modification of the method reported by Mowry (32).

Mucochloric acid (25 g, 148 mmoles) was slurried in 40 ml of ethanol. A second slurry of 20 g (173 mmoles) of semicarbazide hydrochloride in 40 ml of water was prepared. A third slurry of 9.6 g (90 mmoles) of sodium carbonate in 20 ml of water was prepared. None of the three mixtures formed a homogeneous solution. The first two mixtures were then combined at room temperature and stirred with a glass rod. The sodium carbonate mixture was then added with stirring in drops or at such a rate that frothing due to carbon dioxide evolution did not lead to spillage of the product. Massive evolution of carbon dioxide was observed after each addition followed by precipitation of a white solid. The addition and stirring with a glass rod was continued for a period of about 20 minutes during which the addition was completed. Stirring was continued for an ad-

ditional hour. The white slurry was stirred occasionally during the following 2 hour period and allowed to stand for 4 hours. Vacuum filtration with a Büchner funnel gave a near quantitative yield of mucochloric acid semicarbazone (32.4 g, 97% yield) as a white powder after crystallization from ethanol mp 184-185°, lit (32), mp 183°. Mucochloric acid semicarbazone (22.6 g, 100 mmoles) was then refluxed in 140 ml of glacial acetic acid on a heating mantle for 6 hours during which period all the solid dissolved. The dark yellow solution was treated with activated charcoal and filtered hot. The filtrate was diluted to 1 liter with water and cooled. On filtering 15.18 g (92% yield) of 4,5-dichloropyridazin-3(2*H*)-one was collected, mp 200-201°. Mowry (32) reported a yield of 69%, mp 202°. Castle and Seese reported a melting point of 202-203° (33).

Reaction of 2,3-Dichloroquinoxaline with 2-Amino-6-picoline-3-thiol.

2-Amino-6-picoline-3-thiol (**13**) (4.2 g, 30 mmoles) was placed in the reaction flask containing 3 g of sodium hydroxide dissolved in 40 ml of water. The mixture was then warmed to dissolve the reagents. A second solution of 2,3-dichloroquinoxaline (6.97 g, 35 mmoles) in 80 ml of DMF was prepared and added to the above reagents in the reaction flask. The entire mixture was refluxed in an oil bath for 15 hours. At the end of the reflux period, the mixture containing a yellow precipitate was poured into a beaker containing 500 ml of water, stirred and cooled. The crude product was collected by filtration. Fractional crystallization from aqueous DMF (Norit) gave 2,3-bis(2-amino-6-picolinyl-3-thio)quinoxaline (**16**, R = H) (9.38 g, 77% yield) as the first product (**B**), mp >300°; ir: ν max 3289, 3096, 1620, 1558, 1530, 1486, 1440, 1404, 1380, 1340, 1323, 1252, 1227, 1148, 1098, 990, 796, 728, 682, 602, 590, 560, 540, 493, 450, 420 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 2.35 (s, 6′-CH_3, 6″-CH_3), 6.38 (m, 2′-NH_2, 2″-NH_2, 6-H, 7-H), 7.50 (m, 4′-H, 4″-H, 5′-H, 5″-H, 5-H, 8-H); ms: m/e (relative intensity) 95 (32), 106 (27), 112 (20), 139 (75), 140 (35), 234 (16), 235 (13), 265 (12), 266 (22), 267 (100%), 268 (24), 357 (11), 373 (39), 374 (15), 391 (54), 392 (17), 406 (M^+, 72%), 407 (M^+ +1, 25), 408 (M^+ +2, 13).

Anal. Calcd. for $C_{20}H_{18}N_6S_2$: C, 59.11; H, 4.43; N, 20.69; S, 15.76. Found: C, 58.92; H, 4.43; N, 20.58; S, 15.81.

The second product obtained during the fractional crystallization was 2,3-bis(*N,N*-dimethylamino)quinoxaline (**A**) (**15**, R = H) (1.17 g, 18% yield), mp 63.5-64.5°; ir: ν max 2895, 2817, 2740, 1637, 1538, 1527, 1484, 1450, 1429, 1399, 1390, 1359, 1340, 1290, 1245, 1163, 1124, 1089, 1044, 1004, 952, 933, 878, 791, 763, 757, 685, 650, 625, 602, 567, 540, 488, 417 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 3.00 (s, 2-N(CH_3)$_2$′, 7.47 (m, 5-H, 6-H, 7-H, 8-H); ms: m/e (relative intensity) 75 (15), 76 (22), 77 (21), 90 (41), 93 (19), 100 (45), 102 (63), 103 (77), 104 (18), 108 (17), 117 (18), 118 (20), 119 (13), 129 (71), 130 (51), 131 (54), 132 (15), 144 (100), 145 (23), 158 (35), 172 (14), 173 (14), 201 (55), 216 (M^+, 32%), 217 (M^+ +1, 5).

Anal. Calcd. for $C_{12}H_{16}N_4$: C, 66.67; H, 7.41; N, 25.92. Found: C, 66.56; H, 7.42; N, 26.21.

Reaction of 2,3,6-Trichloroquinoxaline with 2-Amino-6-picoline-3-thiol.

To a solution of 5 g of sodium hydroxide in 50 ml of water was added 7.0 g (50 mmoles) of 2-amino-6-picoline-3-thiol. The mixture was warmed on a steam bath until a homogeneous mixture was obtained. A second solution of 12.84 g (55 mmoles) of 2,3,6-trichloroquinoxaline in 100 ml of DMF was prepared and added to the first one. The entire solution was refluxed in an oil bath for 15 hours. It was then diluted to 800 ml with water, cooled and filtered. The impure residue was purified by fractional crystallization from aqueous DMF after treatment with activated charcoal to yield two yellow products. The first product (**A**) that crystallized out as glistening yellow plates was 6-chloro-2,3-bis(*N,N*-dimethylamino)-quinoxaline (**15**, R = Cl) (3.01 g, 24% yield), mp 78-79°; ir: ν max 2900, 2800, 2750, 1626, 1580, 1538, 1493, 1458, 1437, 1393, 1357, 1323, 1276, 1255, 1160, 1136, 1094, 1042, 935, 895, 851, 807, 785, 735, 699, 685, 610, 589, 538, 440, 417 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 3.02 (s, 2-N(CH_3)$_2$, 3-N(CH_3)$_2$), 7.40 (m, 5-H, 7-H, 8-H); ms: m/e (relative intensity) 100 (18), 102 (11), 110 (14), 117 (27), 124 (25), 126 (10), 136 (20), 137 (29), 138 (13), 139 (10), 152 (11), 163 (35), 164 (23), 165 (38), 166 (14), 177 (11), 178 (57), 179 (16), 180 (20), 194 (15), 206 (15), 207 (18), 219 (13), 220 (11), 235 (100), 236 (14), 250 (M^+, 62%), 251 (M^+ +1, 13), 252 (M^+ +2, 21).

Anal. Calcd. for $C_{12}H_{15}ClN_4$: C, 57.49; H, 5.99; N, 22.35; Cl, 14.17. Found: C, 57.47; H, 6.10; N, 22.57; Cl, 14.00.

The second product (**13**) obtained by fractional crystallization of the product from aqueous DMF was 6-chloro-2,3-bis(2-amino-6-picolinyl-3-thio)quinoxaline (**16**, R = Cl), mp 256.5-257.5°; ir: ν max 3283, 3106, 1616, 1558, 1524, 1511, 1475, 1437, 1429, 1380, 1323, 1316, 1250, 1220, 1127, 1095, 1000, 916, 852, 806, 752, 690, 605, 566, 522, 490, 440, 424, 413 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 2.33 (s, 6′-CH_3, 6″-CH_3), 6.41 (m, 2′-NH_2, 2″-NH_2, 5′-H, 5″-H), 7.55 (m, 5-H, 7-H, 8-H, 4′-H, 4″-H); ms: m/e (relative intensity) 93 (41), 95 (49), 98 (24), 105 (19), 106 (38), 112 (27), 139 (100), 140 (63), 268 (17), 299 (14), 300 (19), 301 (89), 302 (25), 303 (38), 333 (11), 391 (11), 407 (37), 408 (13), 409 (17), 425 (57), 426 (18), 427 (28), 440 (M^+, 75%), 441 (M^+ +1, 26), 442 (M^+ +2, 37).

Anal. Calcd. for $C_{20}H_{17}ClN_6S_2$: C, 54.48; H, 3.86; N, 19.07; Cl, 8.06; S, 14.53. Found: C, 54.23; H, 3.90; N, 19.02; Cl, 8.14; S, 14.66.

4-Chloro-5-(3-amino-6-methoxypyridyl-2-thio)pyridazin-3(2*H*)-one (**22**).

3-Amino-6-methoxypyridin-2(1*H*)-thione (**9**) (3.12 g, 20 mmoles) was dissolved in a solution of 5 g of sodium hydroxide in 20 ml of water. A second solution of 4,5-dichloropyridazin-3(2*H*)-one (**21**) (4.95 g, 30 mmoles) in 50 ml of DMSO was prepared. The two solutions were then combined and refluxed with gentle heating in an oil bath for 1 hour. The dark red solution was cooled and diluted with water to 500 ml. Neutralization with glacial acetic acid followed by cooling in ice gave a dark orange-yelow product. Recrystallization from aqueous DMF yielded 4-chloro-5-(3-amino-6-methoxypyridyl-2-thio)pyridazin-3(2*H*)-one (**22**) (3.53 g, 62% yield) as yellow microcrystalline plates, mp 295-296°; ir: ν max 3356, 3155, 3110, 3030, 2970, 2915, 2857, 1642, 1610, 1560, 1538, 1497, 1470, 1415, 1370, 1333, 1294, 1270, 1230, 1172, 1101, 1053, 983, 850, 820, 763, 678, 620, 610, 556, 540, 490, 467 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 3.68 (s, 6′-OCH_3), 5.30 (b, 3-NH_2), 6.77 (d, J = 8.4 Hz, 5′-H), 7.04 (s, 6-H), 7.28 (d, J = 8.4 Hz, 4′-H), 13.23 (s, b, 2-NH); ms: m/e (relative intensity) 97 (9), 111 (12), 114 (6), 141 (8), 149 (5), 205 (10), 206 (17), 233 (9), 234 (48), 248 (34), 249 (100), 250 (19), 251 (6), 284 (M^+, 31%), 285 (M^+ +1, 6), 286 (M^+ +2, 13).

Anal. Calcd. for $C_{10}H_9ClN_4O_2S$: C, 42.18; H, 3.16; N, 19.68; Cl, 12.48; S, 11.25. Found: C, 42.02; H, 3.27; N, 19.63; Cl, 12.51; S, 10.94.

7-Methoxy-2,3,6-triazaphenothiazin-1(2*H*)-one (**23**).

4-Chloro-5-(3-amino-6-methoxypyridyl-2-thio)pyridazin-3(2*H*)-one (**22**) (1.0 g, 3.5 mmoles) was refluxed in 30 ml of concentrated hydrochloric acid in an oil bath for 16 hours. The excess acid was removed by distillation *in vacuo*. The dark red slurry was diluted with ice-cold water and cooled. Neutrallization with concentrated ammonia while cooling gave a dark red product which was collected by fitration. Recrystallization from aqueous DMF after treatment with activated charcoal gave 7-methoxy-2,3,6-triazaphenothiazin-1(2*H*)-one (**23**) (0.71 g, 82% yield) as glittering red needles, mp >300°; ir: ν max 3398 (b), 3300, 3030, 1661, 1613, 1587, 1508, 1443, 1429, 1389, 1350, 1284, 1253, 1235, 1157, 1111, 1053, 1011, 923, 870, 826, 818, 735, 665, 613, 550 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 3.58 (s, 7-OCH_3), 6.81 (d, J = 8.4 Hz, 8-H), 7.14 (d, J = 8.4 Hz, 9-H), 7.82 (s, 4-H), 8.40 (s, 10-NH), 12.50 (s, b, 2-NH); ms: m/e (relative intensity) 166 (6), 178 (4), 191 (4), 205 (13), 206 (11), 219 (5), 233 (4), 247 (7), 248 (M^+, 100%), 249 (M^+ +1, 11), 250 (M^+ +2, 4).

Anal. Calcd. for $C_{10}H_8N_4O_2S$: C, 48.39; H, 3.23; N, 22.58; S, 12.90. Found: C, 48.61; H, 3.48; N, 22.63; S, 12.88.

7-Methoxy-2,3,6-triazaphenothiazin-4(3*H*)-one (**24**).

A slurry of 4-chloro-5-(3-amino-6-methoxypyridyl-2-thio)pyridazin-3(2*H*)-one (**22**) (1.2 g, 4.2 mmoles) in 25 ml of glacial acetic acid was refluxed in an oil bath for 16 hours. The solution was concentrated to near dryness *in vacuo*. About 100 ml of water was then added and the solution neutrallized to *p*H 7 with concentrated ammonia while cooling. The ice-cold slurry was filtered to collect the crude product. Recrystallization from aqueous DMAC after treatment with activated charcoal gave an orange yellow product identified as 7-methoxy-2,3,6-triazaphenothi-

azin-4(3*H*)-one (**24**) (0.93 g, 89% yield) as orange plates; mp >300°; ir: ν max 3376 (b), 3226, 1664, 1634, 1626, 1605, 1580, 1515, 1493, 1477, 1449, 1390, 1540, 1250, 1170, 1111, 1018, 976, 893, 824, 765, 517, 476, 415 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 3.68 (s, 7-OCH_3), 6.34 (d, J = 8.4 Hz, 8-H), 7.17 (d, J = 8.4 Hz, 9-H), 7.25 (s, 1H), 8.50 (s, 10-NH), 12.73 (s, b, 3-NH); ms: m/e (relative intensity) 217 (5), 233 (8), 248 (M^+, 100%), 249 (M^+ +1, 8), 250 (M^+ +2, 3).

Anal. Calcd. for $C_{10}H_8N_4O_2S$: C, 48.39; H, 3.23; N, 22.58; S, 12.90. Found: C, 48.12. H, 3.20; N, 22.47; S, 13.03.

Reaction of 3-Amino-6-methoxypyridine-2(1*H*)-thione (**9**) with 4,5-Dichloropyridazin-3(2*H*)-one (**21**).

3-Amino-6-methoxypyridine-2(1*H*)-thione (**9**) (3.12 g, 20 mmoles) was dissolved in 20 ml of water containing 4 g of sodium hydroxide. A solution of 4,5-dichloropyridazin-3(2*H*)-one (**21**) (3.63 g, 22 mmoles) in 50 ml of dimethyl sulfoxide was added to it and the entire mixture refluxed in an oil bath for 20 hours. At the end of the reflux period, the dark solution was poured onto 600 g of crushed ice and acidified with glacial acetic acid. The precipitate that formed was collected by suction filtration after cooling. The product was redissolved in *N,N*-dimethylformamide (DMF), treated with activated charcoal, filtered and chilled. The yellowish-red product that crystallized out was collected by filtration. Fractional crystallization of this product gave two compounds, 4-chloro-5-(3-amino-6-methoxypyridyl-2-thio)pyridazin-3(2*H*)-one (**22**) (0.74 g, 26% yield) and 7-methoxy-2,3,6-triazaphenothiazin-1(2*H*)-one (**23**) (1.02 g, 41% yield). Mixed melting points of these components with authentic samples **22** and **23** were not depressed and their spectra were superimposable as the case may be.

Acknowledgement.

The authors are grateful to Professor C. Galeffi of Istituto Superiore di Sanita, Rome, Italy for part of the microanalysis and mass spectra. The authors are also indebted to Professor M. L. Lee, Department of Chemistry, Brigham Young University, Provo, Utah, for some of the mass spectra.

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