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Received December 28, 1990

The reaction of 5(4)-amino-4(5)-chloropyridazin-3(2*H*)-ones **1** (**9**) with methyl dithiocarbamates **2** gave 2-arylaminothiazolo[4,5-*d*]pyridazinones **3** (**10**). Treatment of 5(4)-alkylamino-4(5)-chloropyridazin-3(2*H*)-ones **5** (**12**) with **2** afforded the corresponding 2-aryliminothiazolo[4,5-*d*]pyridazinones **6** (**13**). Cyclization of **1a** with phenylisothiocyanate produced 2-amino- and 2-iminothiazolo[4,5-*d*]pyridazinones **3a** and **16**.

J. Heterocyclic Chem., **28**, 859 (1991).

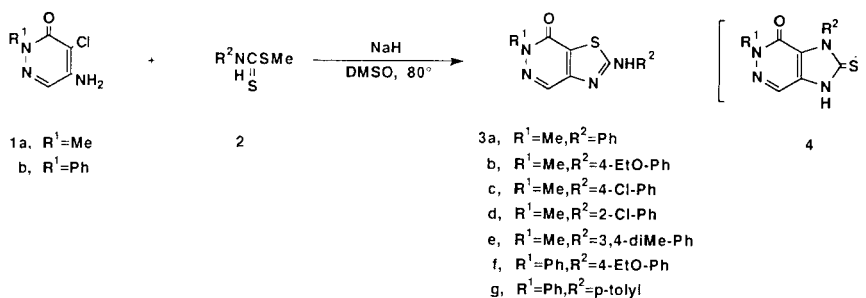
The preparation of thiazolo[4,5-*d*]pyridazin-7(6*H*)-ones has hitherto been developed with various kinds of attractive approaches, because of their potential biological and pharmacological activities [1-5]. Dury reported that the reaction of 5-amidino- and 5-acetylamino-4-chloropyridazinones reacted with hydrogen sulfide to give thiazolo[4,5-*d*]pyridazines [1], while Simiti *et al* reported the preparation of this heterocyclic system from thiazoles and hydrazines. Thiazolo[4,5-*d*]pyridazinones bearing amino groups at C-2, which possess analgesic and anti-inflammatory activities, was first synthesized by Takaya and co-workers by cyclization of 5-amino-6-chloropyridazinones with carbon disulfide, followed by *S*-methylation with methyl iodide and then amination with amines under heating [3]. How-

ever, it is not able to introduce an arylamino group into C-2 by this method, due to the weaker nucleophilicity of arylamines.

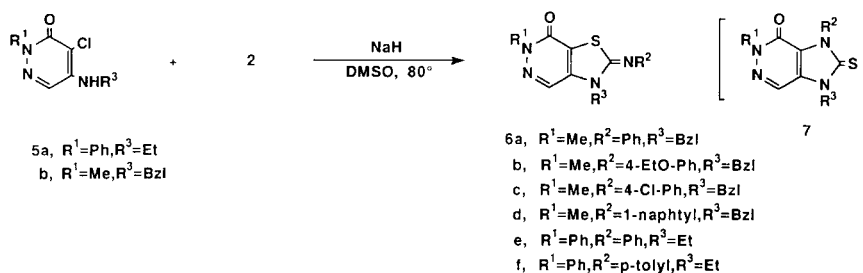
As a continuation of our study on a new synthesis of fused pyridazinones, we investigated the new route for the preparation of 2-arylaminothiazolo[4,5-*d*]pyridazinones from 5(4)-amino-4(5)-chloropyridazin-3(2*H*)-ones and methyl dithiocarbamates. So far there has no report dealing with 2-arylaminothiazolo[4,5-*d*]pyridazinones.

When 5-amino-4-chloropyridazin-3(2*H*)-ones **1** [1,6] were heated with an excess of methyl dithiocarbamates **2** [7-10] in DMSO at 80° in the presence of sodium hydride, 2-arylaminothiazolo[4,5-*d*]pyridazin-7(6*H*)-ones **3** were successfully provided in moderate yields. The ir spectra of **3** show-

Scheme 1



Scheme 2



ed NH at 3270-3250 cm^{-1} and the mass spectra indicated the parent ion peak corresponding to the elimination of methanethiol and hydrogen chloride from the reactant. In this reaction, however, the structural isomer **4** is possible to form as the product by cyclization through *N*-alkylation and the structure of **3** could not be determined by these spectral and elemental data. To confirm the structure of **3**, we measured the ^{13}C -nmr spectra of **3a** in both DMSO-d_6 and the solution added a drop of *N* sodium hydroxide in it, and compared these spectral data. If the structure is isomeric **4**, the high-field shift of the thiocarbonyl carbon at C-2 has to be observed. However, the spectrum hardly changed at 150-200 ppm region. These results supported that the structural assignment of the product as **3** was correct.

Treatment of 5-alkylamino-4-chloropyridazin-3(2*H*)-ones **5** [6,11] with **2** under the same conditions as the preparation of **3** produced 2-aryliminothiazolo[4,5-*d*]pyridazin-7(6*H*)-ones **6** in low yields. All the ir, ^1H -nmr and mass spectral data satisfied the assigned structure **6**. However, these data cannot discriminate between **6** and another possible isomer **7**. Therefore, the hydrolysis of the product **6b** was carried out in concentrated hydrochloric acid-ethanol under reflux to afford 2-oxothiazolo[4,5-*d*]pyridazin-7(6*H*)-one **8** and *p*-phenetidine. This supports the assigned structure **6**.

We also examined the cyclization of 4-amino-5-chloropyridazin-3(2*H*)-one **9**, a regioisomer of **1a**, with **2** under the same conditions, and expectedly obtained the corre-

Table 1
2-Arylaminothiazolo[4,5-*d*]pyridazin-7(6*H*)-ones **3a-g**

No.	R ¹	R ²	Mp (°C)	Yield (%)	IR (cm^{-1})	Mass (M^+)	$^1\text{H-NMR}$ (ppm) (DMSO-d_6)
3a	Me	Ph	266-267 [a]	45	3256 (NH) 1621 (C=O)	258	3.72 (s, 3H, NCH_3), 6.93-7.89 (m, 5H, Ph), 8.31 (s, 5H, CH=), 11.09 (s, 1H, NH)
3b	Me	4-EtOPh	281-282 [a]	69	3260 (NH) 1621 (C=O)	302	1.32 (t, 3H, $J = 7$ Hz, CH_3), 3.70 (s, 3H, NCH_3), 4.02 (q, 2H, $J = 7$ Hz, CH_2), 6.78-7.77 (m, 4H, Ar-H), 8.25 (s, 1H, CH=), 10.85 (s, 1H, NH)
3c	Me	4-ClPh	>300 [a]	48	3274 (NH) 1628 (C=O)	292	3.72 (s, 3H, NCH_3), 7.30-7.94 (m, 4H, Ar-H), 8.31 (s, 1H, CH=), 11.20 (br, 1H, NH)
3d	Me	2-ClPh	259-260 [a]	60	3260 (NH) 1629 (C=O)	292	3.72 (s, 3H, NCH_3), 7.19-7.70 (m, 4H, Ar-H), 8.29 (s, 1H, CH=), 10.67 (br, 1H, NH)
3e	Me	3,4-diMePh	288-289 [a]	55	3266 (NH) 1627 (C=O)	286	2.20 (s, 6H, $\text{CH}_3 \times 2$), 3.71 (s, 3H, NCH_3), 7.04-7.60 (m, 3H, Ar-H), 8.29 (s, 1H, CH=), 10.67 (br, 1H, NH)
3f	Ph	4-EtOPh	207-208 [b]	52	3231 (NH) 1640 (C=O)	364	1.33 (t, 3H, $J = 7$ Hz, CH_3), 4.04 (q, 2H, $J = 7$ Hz, CH_2), 6.85-7.77 (m, 9H, Ph and Ar-H), 8.45 (s, 1H, CH=), 11.00 (s, 1H, NH)
3g	Ph	<i>p</i> -tolyl	243-244 [b]	53	3268 (NH) 1629 (C=O)	334	2.29 (s, 3H, CH_3), 7.10-7.70 (m, 9H, Ph and Ar-H), 8.47 (s, 1H, CH=), 11.07 (s, 1H, NH)

[a] Recrystallization from ethanol-dimethylformamide. [b] Recrystallization from ethanol. **3a** had ^{13}C -nmr (deuteriodimethyl sulfoxide): δ 38.95 (CH_3), 118.49, 123.28 (Ph), 129.05 (CH=), 131.24, 139.56 (Ph), 152.22 (C), 155.95 (C), 167.85 (C); (deuteriodimethyl sulfoxide-sodium hydroxide): δ 38.92 (CH_3), 119.40, 122.62 (Ph), 128.99 (CH=), 130.93, 143.05 (Ph), 153.16 (C), 156.10 (C), 168.91 (C).

Table 1 (Continued)

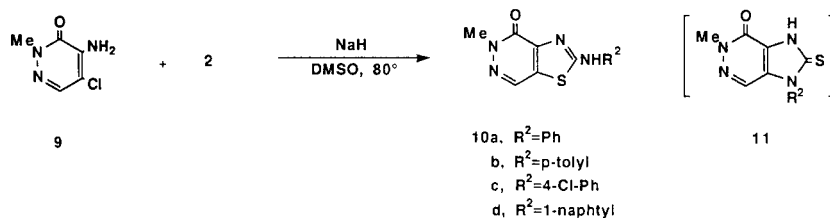
No.	R ¹	R ²	Formula	Analysis (%)		
				Calcd. (Found)		
				C	H	N
3a	Me	Ph	$\text{C}_{12}\text{H}_{10}\text{N}_4\text{OS}$	55.80 (55.95)	3.90 (4.02)	21.69 (21.60)
3b	Me	4-EtOPh	$\text{C}_{14}\text{H}_{14}\text{N}_4\text{O}_2\text{S}$	55.61 (55.52)	4.67 (4.65)	18.53 (18.40)
3c	Me	4-ClPh	$\text{C}_{12}\text{H}_9\text{ClN}_4\text{OS}$	49.23 (49.25)	3.10 (3.27)	19.14 (18.89)
3d	Me	2-ClPh	$\text{C}_{12}\text{H}_9\text{ClN}_4\text{OS}$	49.23 (49.01)	3.10 (3.21)	19.40 (19.02)
3e	Me	3,4-diMePh	$\text{C}_{14}\text{H}_{14}\text{N}_4\text{OS}$	58.72 (58.42)	4.93 (5.06)	19.57 (19.23)
3f	Ph	4-EtOPh	$\text{C}_{19}\text{H}_{16}\text{N}_4\text{O}_2\text{S}$	62.62 (62.36)	4.43 (4.23)	15.37 (15.12)
3g	P	<i>p</i> -tolyl	$\text{C}_{18}\text{H}_{14}\text{N}_4\text{OS}$	64.65 (64.77)	4.22 (4.16)	16.75 (16.69)

sponding 2-arylaminothiazolo[4,5-*d*]pyridazin-4(5*H*)-ones **10** in 53-84% yields. In this reaction, there is a possibility that the product might be a isomeric structural **11** as in the case of **3**, and so the ^{13}C -nmr spectra of **10a** were measured in the same manner as **3** and did not show any changes. This result supports the structural assignment of the product as **10**.

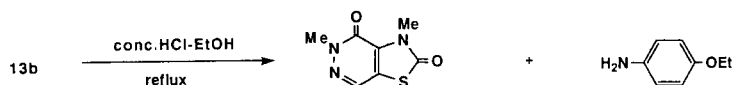
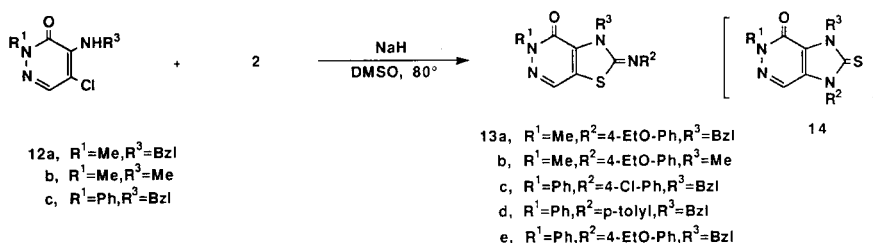
When 4-alkylamino compounds **12** [6,11], a regioisomer of **5**, were heated with **2** in DMSO at 80° , 2-aryliminothiazolo[4,5-*d*]pyridazin-4(5*H*)-ones **13** were expectedly produced in 17-48% yields. Similarly in the case of **6**, discrimination between **13** and the structural isomer **14** was successfully achieved by hydrolysis of the product in concentrated hydrochloric acid-ethanol to 2-oxo compound **15**.

As a new route for the preparation of **3**, we further examined the reaction of **1a** with phenylisothiocyanate. The reaction of **1a** with an equivalent of phenylisothiocyanate

Scheme 3



Scheme 4



15

was successfully carried out in DMSO in the presence of sodium hydride to afford **3a** in 28% yield. The use of two equivalent of phenylisothiocyanate under the same conditions provided **16** in 24% yield along with **3a** in 36% yield. As to the structure of the product **16**, the isomeric structure **17** is also possible. In order to discriminate the

structure **16** and **17**, the hydrolysis of the product was carried out in concentrated hydrochloric acid-ethanol and resulting 2-oxothiazolo[4,5-*d*]pyridazin-7(6*H*)-one **18** was isolated. From these results, the structure of the product is evident to be **16**. The spectral data and the elemental analysis also supported the assigned structure.

Table 2
 2-Aryliminothiazolo[4,5-*d*]pyridazin-7(6*H*)-ones **6**

No.	R ¹	R ²	R ³	Mp (°C)	Yield (%)	IR (cm ⁻¹)	Mass (M ⁺)	¹ H-NMR (ppm) (DMSO- <i>d</i> ₆)
6a	Me	Ph	Bzl	166-168	19	1655 (C=O)	348	3.68 (s, 3H, NCH ₃), 5.39 (s, 2H, CH ₂), 6.88-7.66 (m, 10H, Ph x 2), 8.27 (s, 1H, CH=)
6b	Me	4-EtOPh	Bzl	163	67	1652 (C=O)	392	1.32 (t, 3H, J = 7 Hz, CH ₃), 3.67 (s, 3H, NCH ₃), 4.02 (q, 2H, J = 7 Hz, CH ₂), 5.36 (s, 2H, CH ₂), 6.95 (s, 4H, Ar-H), 7.39 (s, 5H, Ph), 8.26 (s, 1H, CH=)
6c	Me	4-ClPh	Bzl	167-168	36	1650 (C=O)	382	3.68 (s, 3H, NCH ₃), 5.38 (s, 2H, CH ₂), 6.92-7.63 (m, 9H, Ph and Ar-H), 8.30 (s, 1H, CH=)
6d	Me	1-naphtyl	Bzl	176	28	1656 (C=O)	398	3.69 (s, 3H, NCH ₃), 5.54 (s, 2H, CH ₂), 7.08-8.02 (m, 12H, Ph and naphthyl), 8.38 (s, 1H, CH=)
6e	Ph	Ph	Et	155-156	17	1625 (C=O)	348	1.34 (t, 3H, J = 7 Hz, CH ₃), 4.21 (q, 2H, J = 7 Hz, CH ₂), 6.94-7.68 (m, 10H, Ph x 2), 8.55 (s, 1H, CH=)
6f	Ph	<i>p</i> -tolyl	Et	194	22	1646 (C=O)	362	1.36 (t, 3H, J = 7 Hz, CH ₃), 2.30 (s, 3H, CH ₃), 4.20 (q, 2H, J = 7 Hz, CH ₂), 6.82-7.70 (m, 9H, Ph and Ar-H), 8.54 (s, 1H, CH=)

[a] Recrystallization from ethanol.

Table 2 (Continued)

No.	R ¹	R ²	R ³	Formula	Analysis (%)		
					Calcd.	(Found)	
					C	H	N
6a	Me	Ph	Bzl	C ₁₉ H ₁₆ N ₄ OS	65.50 (65.42)	4.63 (4.70)	16.08 (15.98)
6b	Me	4-EtOPh	Bzl	C ₂₁ H ₂₀ N ₄ O ₂ S	64.27 (64.12)	5.14 (5.06)	14.28 (13.83)
6c	Me	4-ClPh	Bzl	C ₁₉ H ₁₅ ClN ₄ OS	59.60 (59.45)	3.95 (4.04)	14.63 (14.37)
6d	Me	1-naphtyl	Bzl	C ₂₃ H ₁₈ N ₄ OS	69.33 (69.53)	4.55 (4.57)	14.06 (13.93)
6e	Ph	Ph	Et	C ₁₉ H ₁₆ N ₄ OS	65.60 (65.62)	4.63 (4.70)	16.08 (15.73)
6e	Ph	<i>p</i> -tolyl	Et	C ₂₀ H ₁₈ N ₄ OS	66.28 (66.03)	5.01 (5.07)	15.46 (15.08)

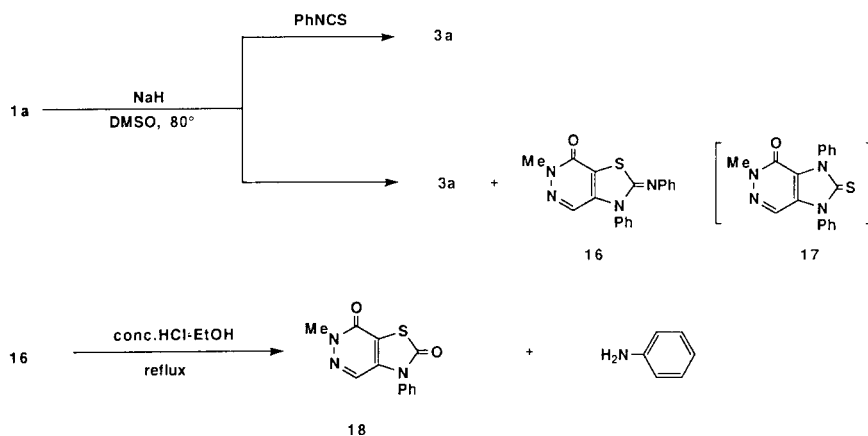
The intramolecular rearrangement with the elimination of isothiocyanic acid provides the final compound **16**.

The application of aminopyridazinone to the preparation of other fused heterocycles is currently being investigated.

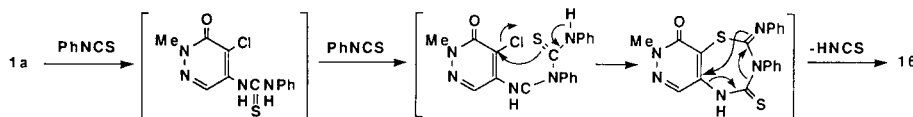
EXPERIMENTAL

All the melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. The ir spectra were recorded with a JASCO IRA-1 grating ir spectrometer. The ¹H-nmr spectra were determined with a HITACHI R-600 spectrometer and the ¹³C-nmr spectra were measured with JEOL-GX 400 spectrometer using tetramethylsilane as an internal standard. Mass spectra were measured with a JEOL JMS-DX 303 mass spectrometer.

Scheme 5



Scheme 6



Probably, the formation pathway of **16** is presumed to be as follows. The reaction proceeds through the initial addition of a molecular phenylisothiocyanate to the amino group at C-5 of **1a**. Further addition of a molecular phenylisothiocyanate to the resulting thiourea to provide thioureido followed by cyclization by the intramolecular S-alkylation forms a seven membered ring intermediate.

Methyl *N*-Aryldithiocarbamate (**2**).

These compounds were prepared by literature methods [7-10]. 5-Amino-4-chloro-2-methylpyridazin-3(2*H*)-one (**1a**) and 4-Amino-5-chloro-2-methylpyridazin-3(2*H*)-one (**9**).

A mixture of 4,5-dichloro-2-methylpyridazin-3(2*H*)-one [1] (14.32 g, 80 mmoles) and 28% ammonium hydroxide (100 ml) was heated at 140-150° for 12 hours in an autoclave. Precipitated

Table 3
2-Arylimino-5-methylthiazolo[4,5-*d*]pyridazin-4(5*H*)-ones **10**

No.	R ²	Mp (°C)	Yield (%)	IR (cm ⁻¹)	Mass (M ⁺)	¹ H-NMR (ppm) (DMSO-d ₆)
10 a	Ph	222-223 [a]	63	3238 (NH) 1634 (C=O)	258	3.73 (s, 3H, NCH ₃), 6.90-7.90 (m, 5H, Ph), 8.40 (s, 1H, CH=), 10.96 (s, 1H, NH)
10 b	<i>p</i> -tolyl	298-299 [b]	84	3228 (NH) 1632 (C=O)	272	2.29 (s, 3H, CH ₃), 3.73 (s, 3H, NCH ₃), 7.04-7.76 (m, 4H, Ar-H), 8.39 (s, 1H, CH=), 10.87 (br, 1H, NH)
10 c	4-ClPh	>300 [b]	53	3240 (NH) 1630 (C=O)	292	3.73 (s, 3H, NCH ₃), 7.25-7.97 (m, 4H, Ar-H), 8.41 (s, 1H, CH=), 11.07 (br, 1H, NH)
10 d	1-naphthyl	286-287 [b]	69	3275 (NH) 1614 (C=O)	308	3.72 (s, 3H, NCH ₃), 7.40-8.32 (m, 7H, naphthyl), 8.36 (s, 1H, CH=), 10.93 (s, 1H, NH)

[a] Recrystallization from ethanol. [b] Recrystallization from ethanol-dimethylformamide. **10a** had ¹³C-nmr (deuteriodimethyl sulfoxide): δ 39.34 (CH₃), 118.15, 122.92 (Ph), 128.38 (C), 129.05 (CH=), 130.93, 139.83 (Ph), 147.20 (C), 155.10 (C), 166.06 (C); (deuteriodimethyl sulfoxide-sodium hydroxide): δ 39.34 (CH₃), 118.15, 122.92 (Ph), 128.38 (C), 129.05 (CH=), 130.93, 139.83 (Ph), 147.20 (C), 155.10 (C), 166.06 (C).

Table 3 (Continued)

No.	R ²	Formula	Analysis (%)		
			Calcd.	Found	
			C	H	N
10 a	Ph	C ₁₂ H ₁₀ N ₄ OS	55.80 (55.85)	3.90 (3.93)	21.69 (21.60)
10 b	<i>p</i> -tolyl	C ₁₃ H ₁₂ N ₄ OS	57.34 (57.44)	4.44 (4.37)	20.57 (20.23)
10 c	4-ClPh	C ₁₂ H ₉ ClN ₄ OS	49.23 (49.31)	3.10 (3.30)	19.14 (18.83)
10 d	1-naphthyl	C ₁₆ H ₁₂ N ₄ OS	62.32 (62.05)	3.92 (4.10)	18.17 (17.81)

solid was filtered and recrystallized from ethanol to give **1a** (5.10 g, 40%), mp 204-205 (lit [1] mp 203-204°).

The filtrate was evaporated to dryness. The residue was dissolved in 6*N* hydrochloric acid (100 ml) and the solution was washed with chloroform (100 ml). The aqueous layer was made alkaline with dilute sodium hydroxide and extracted with chloroform (3 x 50 ml). After removal of chloroform, the residue was purified by recrystallization from ethanol to give **9** (1.2 g, 9%), mp 113°; ir (potassium bromide): ν max cm⁻¹ 3404, 3320 (NH), 1622 (C=O); ¹H-nmr (DMSO-d₆): δ 3.58 (s, 3H, NCH₃), 6.65 (br, 2H, NH₂), 7.67 (s, 1H, CH=); ms: m/z 159 (M⁺).

Anal. Calcd. for C₅H₆ClN₃O: C, 37.63; H, 3.79; N, 26.33. Found: C, 37.42; H, 3.84; N, 25.92.

Table 4
2-Aryliminothiazolo[4,5-*d*]pyridazin-4(5*H*)-ones **13**

No.	R ¹	R ²	R ³	Mp (°C) [a]	Yield (%)	IR (cm ⁻¹)	Mass (M ⁺)	¹ H-NMR (ppm)
13 a	Me	4-EtOPh	Bzl	121	46	1638 (C=O)	392	solvent: deuteriochloroform 1.37 (t, 3H, J = 6 Hz, CH ₃), 3.76 (s, 3H, NCH ₃), 3.98 (q, 2H, J = 6 Hz, CH ₂), 5.79 (s, 2H, CH ₂), 6.87 (s, 4H, Ar-H), 7.14-7.69 (m, 6H, Ph and CH=)
13 b	Me	4-EtOPh	Me	174-175	48	1630 (C=O)	316	solvent: DMSO-d ₆ 1.29 (t, 3H, J = 7 Hz, CH ₃), 3.66 (s, 3H, NCH ₃), 3.82 (s, 3H, NCH ₃), 3.99 (q, 2H, J = 7 Hz, CH ₂), 6.91 (s, 4H, Ar-H), 8.08 (s, 1H, CH=)
13 c	Ph	4-ClPh	Bzl	167-168	30	1644 (C=O)	444	solvent: deuteriochloroform 5.89 (s, 2H, CH ₂), 6.80-7.91 (m, 14H, Ph x 2 and Ar-H), 7.94 (s, 1H, CH=)
13 d	Ph	<i>p</i> -tolyl	Bzl	178	19	1650 (C=O)	424	solvent: DMSO-d ₆ 2.25 (s, 3H, CH ₃), 5.69 (s, 2H, CH ₂), 6.75-7.61 (m, 14H, Ph x 2 and Ar-H), 8.30 (s, 1H, CH=)
13 e	Ph	4-EtOPh	Bzl	167	26	1640 (C=O)	454	solvent: deuteriochloroform 1.41 (t, 3H, J = 7 Hz, CH ₃), 4.03 (q, 2H, CH ₂), 5.83 (s, 2HY, CH ₂), 6.93 (s, 4H, Ar-H), 7.22-7.72 (m, 10H, Ph x 2), 7.83 (s, 1H, CH=)

[a] Recrystallization from ethanol.

Table 4 (Continued)

No.	R ¹	R ²	R ³	Formula	Analysis (%)		
					Calcd. (Found)		
					C	H	N
13 a	Me	4-EtOPh	Bzl	C ₂₁ H ₂₀ N ₄ O ₂ S	64.27 (63.79)	5.14 (5.06)	14.28 (13.96)
13 b	Me	4-EtOPh	Me	C ₁₅ H ₁₆ N ₄ O ₂ S	56.95 (57.21)	5.10 (5.06)	17.71 (17.67)
13 c	Ph	4-ClPh	Bzl	C ₂₄ H ₁₇ ClN ₄ O ₂ S	64.79 (64.44)	3.85 (3.71)	12.59 (12.67)
13 d	Ph	<i>p</i> -tolyl	Bzl	C ₂₅ H ₂₀ N ₄ O ₂ S	70.73 (70.33)	4.75 (4.83)	13.20 (12.96)
13 e	Ph	4-EtOPh	Bzl	C ₂₆ H ₂₂ N ₄ O ₂ S	68.70 (68.61)	4.88 (4.79)	12.33 (12.33)

2-Arylaminothiazolo[4,5-*d*]-pyridazin-7(6*H*)-one (3).

To a solution of **2** (15 ml) and 60% sodium hydride (0.60 g, 15 mmoles) in anhydrous dimethyl sulfoxide (30 ml) was added **1** (10 mmoles). The solution was stirred for 12 hours at 80° under an argon atmosphere. The reaction mixture was poured into the cold water (300 ml) and the separated crystals were filtered. The crude product was recrystallized from appropriate solvents. The results are summarized in Table 1.

2-Aryliminothiazolo[4,5-*d*]pyridazin-7(6*H*)-one (6).

Compound **5** (10 mmoles) was heated with **2** (15 mmoles) for 24-48 hours in the same manner as described for the preparation of **3**. The crude product **6** was recrystallized from ethanol. The results are shown in Table 2.

Hydrolysis of 6b.

A solution of **6b** (0.78 g, 2 mmoles) in concentrated hydrochloric acid (15 ml) and ethanol (15 ml) was refluxed for 2 days. After removal of ethanol, the residue was treated with water and extracted with chloroform (2 x 20 ml). The extract was dried over anhydrous magnesium sulfate, evaporated to dryness and the crude product was recrystallized from ethanol to afford **8** (0.34 g, 62%), mp 118-120°; ir (potassium bromide): ν max cm⁻¹ 1695, 1640 (C=O); ¹H-nmr (DMSO-*d*₆): δ 3.71 (s, 3H, NCH₃), 5.22 (s, 2H, CH₂), 7.35 (s, 5H, Ph), 8.34 (s, 1H, CH=); ms: *m/z* 273 (M⁺).

Anal. Calcd. for C₁₃H₁₁N₃O₂S: C, 57.14; H, 4.06; N, 15.37. Found: C, 57.27; H, 4.11; N, 15.25.

The aqueous layer was neutralized with *N* sodium hydroxide and extracted with chloroform (2 x 20 ml). The extract was dried over anhydrous magnesium sulfate and evaporated to give *p*-phenetidine.

4-Arylaminothiazolo[4,5-*d*]pyridazin-4(5*H*)-one (10).

These compounds were prepared from **9** and **2** in the same manner described for the preparation of **3**. The results are shown in Table 3.

5-Chloro-2-methyl-4-methylaminopyridazin-3(2*H*)-one (12b).

A mixture of 4,5-dichloro-2-methylpyridazin-3(2*H*)-one (13.06 g, 73 mmoles) and 40% aqueous methylamine solution (100 ml) was heated at 130° for 12 hours in an autoclave. After cooling the reaction mixture, the precipitated solid was filtered and recrystallized from 60% aqueous ethanol to give **12b** (2.20 g, 18%), mp 141-142°; ir (potassium bromide): ν max cm⁻¹ 3310 (NH), 1630

(C=O); ¹H-nmr (deuteriochloroform): δ 3.22 (d, 3H, J = 5 Hz, NHCH₃), 3.62 (s, 3H, NCH₃), 5.80 (br, 1H, NH), 7.36 (s, 1H, CH=); ms: *m/z* 173 (M⁺).

Anal. Calcd. for C₆H₈ClN₃O: C, 41.51; H, 4.64; N, 24.20. Found: C, 41.61; H, 4.55; N, 24.07.

The filtrate of the recrystallization was evaporated under reduced pressure and the residue was purified by recrystallization from ethanol to afford 4-chloro-2-methyl-5-methylaminopyridazin-3(2*H*)-one (6.0 g, 48%), mp 161-162°; ir (potassium bromide): ν max cm⁻¹ 3350 (NH), 1640 (C=O); ¹H-nmr (deuteriochloroform): δ 3.04 (d, 3H, J = 6 Hz, NHCH₃), 3.74 (s, 3H, NCH₃), 4.83 (br, 1H, NH), 7.55 (s, 1H, CH=); ms: *m/z* 173 (M⁺).

Anal. Calcd. for C₆H₈ClN₃O: C, 41.51; H, 4.64; N, 24.20. Found: C, 41.36; H, 4.61; N, 24.06.

2-Aryliminothiazolo[4,5-*d*]pyridazin-4(5*H*)-one (13).

Compound **12** (10 mmoles) was allowed to react with **2** (15 mmoles) for 24-48 hours in the same manner as described for the preparation of **3**. The results are summarized in Table 4.

Hydrolysis of 13b.

Compound **13b** (0.63 g, 2 mmoles) was hydrolyzed in the same manner as described above for the hydrolysis of **6b** to give **15** (0.16 g, 41%), mp 184-185°; ir (potassium bromide): ν max cm⁻¹ 1695, 1600 (C=O); ¹H-nmr (deuteriochloroform): δ 3.80 (s, 3H, NCH₃), 3.86 (s, 3H, NCH₃), 7.85 (s, 1H, CH=); ms: *m/z* 197 (M⁺).

Anal. Calcd. for C₇H₇N₃O₂S: C, 42.63; H, 3.58; N, 21.31. Found: C, 42.83; H, 3.55; N, 21.24.

2-Anilino-6-methylthiazolo[4,5-*d*]pyridazin-7(6*H*)-one (3a).

To a solution of phenylisothiocyanate (1.20 ml, 10 mmoles) and 60% sodium hydride (0.40 g, 10 mmoles) in anhydrous dimethyl sulfoxide (30 ml) was added **1a** (1.60 g, 10 mmoles). The solution was stirred for 12 hours at 80° under argon atmosphere. The reaction mixture was poured into the cold water (300 ml) and the separated crystals were filtered. The crude product was recrystallized from ethanol-dimethylformamide to give **3a** (0.72 g, 28%).

6-Methyl-3-phenyl-2-phenyliminothiazolo[4,5-*d*]pyridazin-7(6*H*)-one (16).

A mixture of **1a** (0.96 g, 6 mmoles), phenylisothiocyanate (1.44 ml, 12 mmoles) and 60% sodium hydride (0.48 g, 12 mmoles) was treated in the same manner as described above for **3a**. After heating at 80° for 4 hours, the solution was evaporated *in vacuo* and chloroform (100 ml) was added to the residue. The insoluble solid was filtered to give **3a** (0.56 g, 36%). On the other hand, after evaporation of the filtrate under reduced pressure, the residue was chromatographed on a silica gel column with chloroform as eluent to give **16** (0.48 g, 24%), mp 238-239°; ir (potassium bromide): ν max cm⁻¹ 1655 (C=O); ¹H-nmr (DMSO-*d*₆): δ 3.70 (s, 3H, NCH₃), 6.84-7.78 (m, 11H, Ph x 2 and CH=); ms: *m/z* 334 (M⁺).

Anal. Calcd. for C₁₈H₁₄N₄O₂S: C, 64.65; H, 4.22; N, 16.75. Found: C, 64.68; H, 4.29; N, 16.62.

Hydrolysis of 16.

Compound **16** (0.67 g, 2 mmoles) was hydrolyzed in the same manner as described for the hydrolysis of **6b** to give 6-methyl-3-phenylthiazolo[4,5-*d*]pyridazine-2,7(6*H*)-dione **20** (0.30 g, 58%), mp 242°; ir (potassium bromide): ν max cm⁻¹ 1658, 1622 (C=O); ¹H-nmr (DMSO-*d*₆): δ 3.72 (s, 3H, NCH₃), 7.50-7.71 (m, 6H, Ph and

CH=); ms: m/z 259 (M⁺).

Anal. Calcd. for C₁₂H₉N₃O₂S: C, 55.59; H, 3.50; N, 16.21.
Found: C, 55.88; H, 3.39; N, 16.18.

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