Synthesis of Novel Acyclonucleosides. Reactions of 1-(1-Bromo or 3-Bromo-2-oxopropyl)pyridazin-6-ones

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Reaction of 1-(3-bromo-2-oxopropyl)pyridazin-6-ones **1** and **2** with sodium azide at room temperature gave the corresponding 1-(3-azido-2-oxopropyl)pyridazin-6-ones **3** and **4**, whereas reaction of 1-(1-bromo-2-oxopropyl)pyridazin-6-ones **5** and **6** with excess sodium azide afforded 4-azido-5-chloropyridazin-6-one **7** and 4,5-diazido-3-nitropyridazin-6-one **8** by dealkylation. Some 1-(2-hydroxypropyl)pyridazin-6-ones **9**, **10**, **11** were synthesized from the corresponding 1-(2-oxopropyl) derivatives **1**, **2**, **3**. 4,5-Dichloro-1-(2,3-dihydroxypropyl)-pyridazin-6-one **13** was also prepared from compound **9** *via* the corresponding 2,3-epoxypropyl derivative **12**. Treatment of compound **5** with thiourea gave 4,5-dichloro-1-(2-amino-4-methylthiazol-5-yl)pyridazin-6-one **14**. Reaction of compounds **1** and **2** with thiourea at 20° afforded the corresponding 3-formamidinylthio-2-oxopropyl derivatives **15** and **16**, whereas treatment of compound **1** with thiourea at 45° gave 4,5-dichloro-1-[(2-aminothiazol-5-yl)methyl]pyridazin-6-one **17**. Compound **17** was also prepared from compound **15** by refluxing in ethanol.

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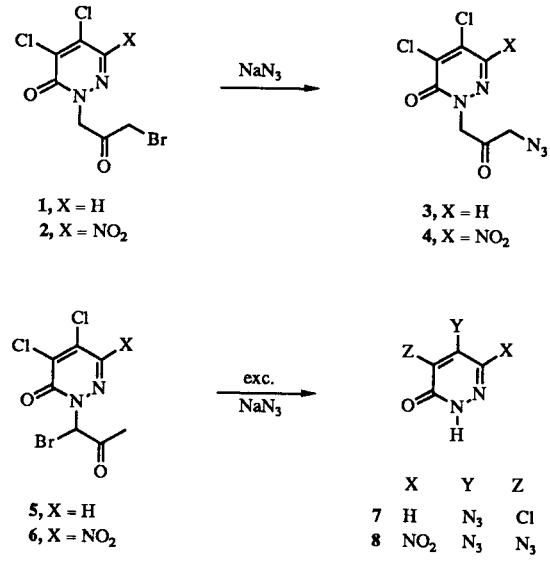
In recent years, major efforts have been directed by nucleoside researchers toward the synthesis of acyclonucleosides with various side chains and aglycones. In addition, the skeletal modification of the heterocyclic portion and/or alkanol side chain of acyclonucleosides have provided numerous azine nucleosides possessing a wide variety of biological actions [1].

As a part of a study on novel acyclonucleosides, we synthesized multisubstituted 1-(2-oxopropyl)pyridazin-6-ones [2] and the corresponding 1-(1-bromo or 3-bromo-2-oxopropyl)pyridazin-6-ones [3].

In this present paper, we report the reactions of multisubstituted 1-(1-bromo or 3-bromo-2-oxopropyl)pyridazin-6-ones with sodium azide and thiourea, and also the synthesis of some 1-(2-hydroxy or 2,3-dihydroxypropyl)pyridazin-6-ones.

Reaction of compounds **1** and **2** with sodium azide in acetone-dimethylformamide (7:1 v/v, for **1**) or tetrahydrofuran (for **2**) at room temperature gave the corresponding 1-(3-azido-2-oxopropyl)pyridazin-6-ones **3** and **4** in excellent yield, whereas reaction of compounds **5** and **6** with excess sodium azide in acetone-dimethylformamide (9:1 v/v) at room temperature furnished the corresponding 4-azidopyridazin-6-one **7** and 4,5-diazidopyridazin-6-one **8** by the dealkylation on the N_1-position of pyridazine ring, respectively. However, we did not obtain the corresponding 1-azido-2-oxopropyl derivatives. The position of azido group for compounds **7** and **8** was proved by further reactions of these compounds [4]. The infrared spectra of compounds **3** and **4** showed two carbonyl and one azido absorption peaks. In the proton magnetic resonance spectra of these compounds were observed two methylene proton signals (NCH_2C, 5.08 for **3** and 5.10 for **4**, CCH_2N_3, 4.00 for **3** and 4.10 for **4**). On the other hand, the infrared spectra of compounds **7** and **8** showed an absorption peak of the azido group at 2176 cm^{-1} for **7** and at 2136 cm^{-1} for **8** and one carbonyl absorption peak at 1664 cm^{-1} for **7** and at 1654 cm^{-1} for **8**. Also, in the proton magnetic resonance spectrum of **7** was observed two proton signals [7.90 (s, 1H), 13.5 (bs, NH, deuterium oxide exchangeable)] and for **8** was shown one proton signal [12.5-15.0 (bs, NH, deuterium oxide exchangeable)]. Further work including the mechanism of the dealkylation for these compounds is under way in our laboratory.

Scheme I



1, X = H
2, X = NO_2

3, X = H
4, X = NO_2

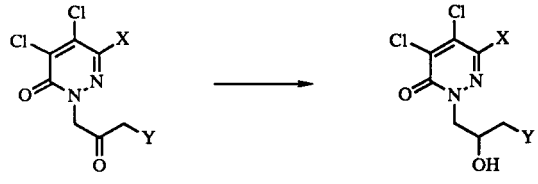
5, X = H
6, X = NO_2

	X	Y	Z
7	H	N_3	Cl
8	NO_2	N_3	N_3

We also attempted the synthesis of some 1-(2-hydroxy or 2,3-dihydroxypropyl)pyridazin-6-ones from the corresponding 1-(2-oxopropyl)pyridazin-6-ones by the selective reduction on the 2'-position. Reduction of compounds **1**, **2** and **3** with sodium borohydride in aqueous tetrahydrofuran gave the corresponding 1-(2-hydroxypropyl)pyri-

dazin-6-ones **9**, **10** and **11** in excellent yield. The infrared spectra of compounds **9-11** showed an absorption peak of the hydroxy group and one carbonyl peak of the pyridazine ring, but the carbonyl peak of the 2-oxopropyl moiety was not detected. Also the infrared spectrum of **11** showed an absorption peak of the azido group at 2100 cm^{-1}. Proton magnetic resonance spectra of compounds **9** and **11** exhibited three proton signals [for **9**, 7.98 (s, $1H_3$), 4.32-4.20 (m, $2H_1' + 1H_2' + OH$), 3.52 (d, J = 4 Hz, $2H_3'$); for **11**, 7.72 (s, $1H_3$), 4.20 (m, $2H_1' + 1H_2'$), 3.42 (m, $2H_3 + OH$)]. And likewise in compound **10** was observed three proton signals [4.40 (m, $2H_1' + 1H_2'$), 3.50 (d, J = 4 Hz, $2H_3'$), 2.80 (bs, OH, deuterium oxide exchangeable)].

Scheme II

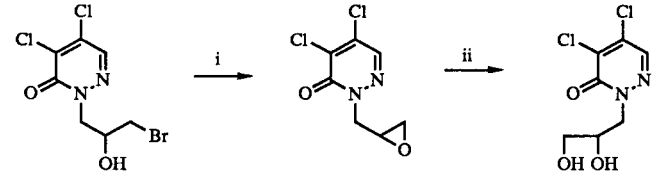


	X	Y
1	H	Br
2	NO_2	Br
3	H	N_3

	X	Y
9	H	Br
10	NO_2	Br
11	H	N_3

Treatment of compound **9** with 10% aqueous sodium hydroxide in tetrahydrofuran at room temperature furnished the corresponding 1-(2,3-epoxypropyl)pyridazin-6-one **12** in 89% yield. Likewise the reaction of **12** with water in the presence of hydrochloric acid in tetrahydrofuran at room temperature gave the corresponding 2,3-dihydroxypropyl derivative **13** in 56% yield. The infrared spectrum of **12** showed only one carbonyl absorption at 1670 cm^{-1}. The proton magnetic resonance spectrum of **12** exhibited four proton signals [7.90 (s, $1H_3$), 4.22 (m, $2H_1'$), 3.38 (m, $1H_2'$) and 2.70 (m, $2H_3'$)]. The infrared spectrum of **13** also showed only one carbonyl absorption peak at 1665 cm^{-1} and an absorption peak of the hydroxy group at about 3450 cm^{-1}. The proton magnetic resonance spectrum of **13** showed three proton signals [7.80 (s, $1H_3$), 4.20 (m, $2H_1' + 1H_2'$) and 3.90-3.20 (m, $2H_3' + 2OH$)].

Scheme III



9 **12** **13**

i) KOH, H_2O; ii) HCl/H_2O, THF

On the other hand, the reaction of compound **1** with thiourea in tetrahydrofuran at 45° gave compound **14** in 54% yield. The infrared spectrum of **14** showed one carbonyl absorption at 1652 cm^{-1} and absorption peaks of the amino group at 3372 and 3288 cm^{-1}. Also in the proton magnetic resonance spectrum of **14** was observed three proton signals [1.84 (s, CH_3), 6.80-7.50 (bs, NH_2) and 8.14 (s, $1H_3$)]. Treatment of the 3'-bromo compounds **1** and **2** with thiourea in tetrahydrofuran at 20° furnished 3-formamidinylthio-2-oxopropyl derivatives **15** and **16** in 50% and 54% yield, respectively. The infrared spectra of **15** and **16** showed two carbonyl absorption peaks and also absorption peaks of the amino group. The proton magnetic resonance spectrum of **15** exhibited four proton signals [2.20 (s, $2H_3'$), 3.20 (bs, NH), 5.10 (m, $2H_1'$), 7.98 (s, $1H_3$)], but the proton signals of NH_2 was not detected. Compound **16** showed four proton signals [2.0 (s, $2H_3'$), 3.60 (bs, NH), 5.28 (s, $2H_1'$), 6.24 (bs, NH_2)]. The reaction of

Table 1

^{1}H-NMR Data of Compounds **3, 4, 7, 8** and **9-17**

Compound	Solvent [c]	δ (ppm)
3	A	4.00 (m, $2H_3'$), 5.08 (m, $2H_1'$), 7.76 (s, $1H_3$)
4	A	4.10 (m, $2H_3'$), 5.10 (m, $2H_1'$)
7	A+B	7.90 (s, $1H_3$), 13.50 (bs, NH, deuterium oxide exchangeable)
8	A	12.50-15.0 (bs, NH, deuterium oxide exchangeable)
9	C	3.52 (d, J = 4 Hz, $2H_3'$), 4.20-4.32 (m, $2H_1' + 1H_2' + OH$ [a], 7.98 (s, $1H_3$)
10	A	2.80 (bs, OH, deuterium oxide exchangeable), 3.50 (d, J = 4.0 Hz, $2H_3'$), 4.40 (m, $2H_1' + 1H_2'$)
11	A+B	3.42 (m, $2H_3' + 10H$) [a], 4.2 (m, $2H_1' + 1H_2'$), 7.72 (s, $1H_3$)
12	A	2.70 (m, $2H_3'$), 3.38 (m, $1H_2'$), 4.22 (m, $2H_1'$), 7.90 (s, $1H_3$)
13	B	3.20-3.90 (m, $2H_3' + 20H$) [a], 4.20 (m, $2H_1' + 1H_2'$), 7.80 (s, $1H_3$)
14	A+B	1.84 (s, CH_3), 6.80-7.50 (bs, NH_2, deuterium oxide exchangeable), 8.14 (s, $1H_3$)
15	C	2.20 (s, $2H_3'$), 3.2 (bs, NH, deuterium oxide exchangeable), 5.10 (m, $2H_1'$), 7.98 (s, $1H_3$) [b]
16	C	2.00 (s, $2H_3'$), 3.60 (bs, NH, deuterium oxide exchangeable), 5.28 (s, $2H_1'$), 6.24 (bs, NH_2, deuterium oxide exchangeable)
17	A+B	5.24 (s, CH_2), 6.84 (s, 1H), 8.02 (s, $1H_3$), 7.00-9.00 (bs, NH_2, deuterium oxide exchangeable)

[a] The proton signal of the OH group was detected by treatment of deuterium oxide. [b] The NH_2 was not observed. [c] A = Deuteriochloroform, B = DMSO-d_6, C = Acetone-d_6.

Scheme IV

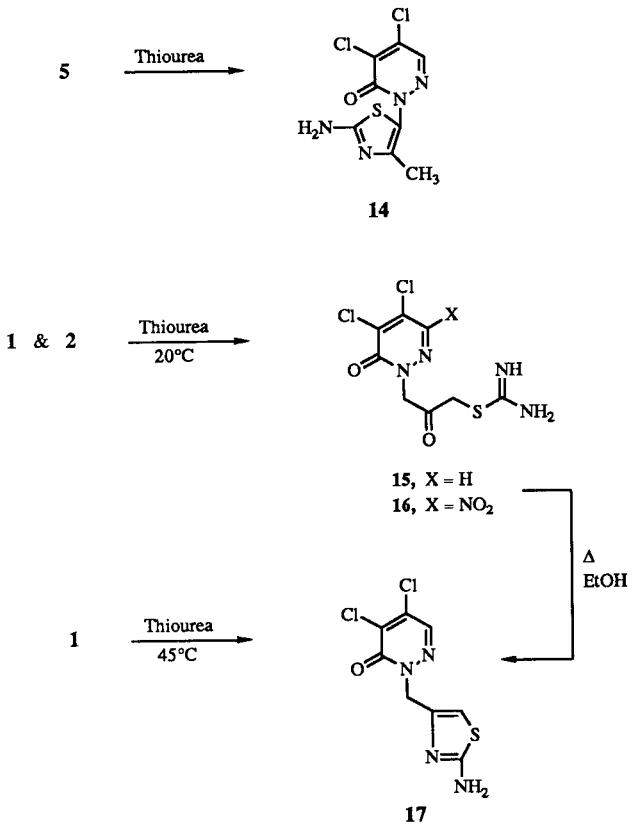


Table 2

Elemental Analysis of Compound **3**, **4**, **7**, **8** and **9-17**

Compound No.	Molecular Formula	Calcd/Found(%) C	H	N
3	$C_7H_5N_5O_2Cl_2$	32.08	1.92	26.73
		32.10	1.61	26.70
4	$C_7H_4N_6O_4Cl_2$	27.38	1.31	27.37
		27.31	1.42	27.39
7	$C_4H_2N_5OCl$	28.01	1.18	40.83
		27.85	1.21	40.60
8	$C_4HN_9O_3$	21.53	0.45	56.60
		21.55	0.48	56.49
9	$C_7H_7N_2O_2Cl_2Br$	27.84	2.34	9.28
		27.90	2.51	9.01
10	$C_7H_6N_3O_4Cl_2Br$	24.23	1.74	12.11
		24.52	1.81	11.98
11	$C_7H_7N_5O_2Cl_2$	31.84	2.67	26.52
		31.98	2.98	26.17
12	$C_7H_6N_2O_2Cl_2$	38.04	2.74	12.67
		37.83	2.95	12.32
13	$C_7H_8N_2O_3Cl_2$	35.17	3.37	11.72
		35.20	3.74	11.52
14	$C_8H_6N_4OSCl_2$	34.67	2.18	20.22
		34.83	2.42	20.10
15	$C_8H_8N_4O_2Cl_2S$	32.56	2.73	18.98
		32.60	2.68	19.03
16	$C_8H_7N_5O_4Cl_2S$	28.25	2.07	20.59
		28.20	2.13	20.47
17	$C_8H_6N_4OSCl_2$	34.67	2.18	20.22
		34.80	2.36	20.56

compound **1** with thiourea in tetrahydrofuran or ethanol at 45° afforded 4,5-dichloro-1-[(2-aminothiazol-5-yl)methyl]pyridazin-6-one (**17**) in 72% yield. The infrared spectrum of **17** showed one carbonyl absorption peak at 1664 cm^{-1} and absorption peaks of the amino group at 3400 and 3200 cm^{-1}. The proton magnetic resonance spectrum of **17** showed four proton signals [5.24 (s, CH_2), 6.84 (s, 1H), 8.02 (s, $1H_3$), 7.0-9.0 (bs, NH_2)]. Compound **15** was refluxed for 20 minutes in ethanol to give compound **17** in 72% yield. Analytical data of this compound was identical with the data of the product by method A.

Further work including biological activity is under way in our laboratory.

EXPERIMENTAL

Melting points were determined with a Fisher-Johns apparatus and are uncorrected. Proton nuclear magnetic resonance spectra were obtained on a Bruker AW-80 MHz spectrometer with chemical shift values reported in δ units (parts per million) relative to an internal standard (tetramethylsilane). Mass spectra were obtained from the Korean Research Institute of Chemical Technology (Taejon, Korea). Infrared spectra were obtained on a Hitachi 270-50 spectrophotometer. Elemental analysis were performed with a LECO Micro Carbon Hydrogen Determinator (CHN-800). Open-bed column chromatography was carried out on silica gel 60 (70-230 mesh. Merck) using gravity flow. The columns were packed as slurries with the elution solvent.

4,5-Dichloro-1-(3-azido-2-oxopropyl)pyridazin-6-one (**3**).

A mixture of **1** (0.30 g, 1.0 mmole) [3], sodium azide (0.07 g, 1.1 mmoles), acetone (7 ml) and dimethylformamide (1 ml) was stirred for 5 hours at room temperature. After the solvent was evaporated under reduced pressure, distilled water (30 ml) was added to the residue. The resulting precipitate was filtered, and recrystallized from carbon tetrachloride-dichloromethane (4:1 v/v) to give compound **3** as a white powder in 91% (0.24 g), mp 132-133°; ir (potassium bromide): 3008, 2116, 1734, 1654, 1574 cm^{-1}.

4,5-Dichloro-3-nitro-(3-azido-2-oxopropyl)pyridazin-6-one (**4**).

A mixture of **2** (0.35 g, 1.0 mmole) [3], sodium azide (0.07 g, 1.1 mmoles) and tetrahydrofuran (7 ml) was stirred for 14 hours at room temperature. After the solvent was evaporated under reduced pressure, distilled water (20 ml) was added to the residue. And the mixture was then stirred for 10 minutes at room temperature. The product was extracted with dichloromethane (20 ml x 3). After the organic layer was dried over anhydrous magnesium sulfate, the solution was concentrated to 10 ml under reduced pressure to give compound **4** as yellow crystal in 94% (0.29 g) yield. Recrystallization of a small sample from methylene chloride furnished an analytical sample, mp 110-111°; ir (potassium bromide): 3000, 2110, 1750, 1684, 1586 cm^{-1}.

4-Azido-5-chloropyridazin-6-one (**7**).

A mixture of **5** (1.35 g, 4.5 mmoles), acetone (10 ml) and dimethylformamide (1 ml) was stirred for 5 minutes at room temperature. Sodium azide (0.9 g, 13.8 mmoles) was then added to the above solution. The resulting mixture was stirred for 8 hours at room temperature. After the solvent was distilled off, the product was extracted with ethyl acetate (50 ml x 3). The ester layer was dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to give compound **7** as a yellow powder in 78% (0.6 g) yield. Recrystallization of a small sample from chloroform-cyclohexane (6:4 v/v) furnished an analytical sample, mp 150° dec; ir (potassium bromide): 3034, 2176, 1664, 1389 cm^{-1}; ms: m/e 171 (M^+).

4,5-Diazido-3-nitropyridazin-6-one (**8**).

A mixture of **6** (3.03 g, 8.78 mmoles), acetone (10 ml) and dimethylformamide (2 ml) was stirred for 5 minutes at room temperature. Sodium azide (1.71 g, 26.3 mmoles) was then added to the above solution. The mixture was stirred for 6 hours at room temperature. After the solvent was evaporated under reduced pressure at room temperature, the mixture was then poured into water (50 ml). The product was extracted with ethyl acetate (50 ml x 3). The ester layer was dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to give compound **8** as a yellow powder in 92% (1.8 g) yield. Recrystallization of a small sample from methylene chloride-methanol-cyclohexane (5:1:10 v/v) gave a product of mp 115-118°; ir (potassium bromide): 3140, 2136, 1654, 1368 cm^{-1}; ms: m/e 223 (M^+).

4,5-Dichloro-1-(3-bromo-2-hydroxypropyl)pyridazin-6-one (**9**).

A mixture of **1** (1.0 g. 3.3 mmoles), tetrahydrofuran (10 ml), sodium borohydride (40 mg, 1.1 mmoles) and distilled water (0.2 ml) was stirred for 4 hours at room temperature then acetone (1 ml) was added to the above mixture. The reaction mixture was stirred for an additional 10 minutes at the same temperature. After the solvent was evaporated under reduced pressure, water (20 ml) was added and the product was then extracted with dichloromethane (20 ml x 2). The organic layer was dried over anhydrous magnesium sulfate. After the solvent was evaporated under reduced pressure, the resulting residue was recrystallized from carbon tetrachloride to give compound **9** as colorless crystals in 99% (0.98 g) yield, mp 99-100°; ir (potassium bromide): 3480, 2940, 1652, 1584 cm^{-1}.

4,5-Dichloro-3-nitro-1-(3-bromo-2-hydroxypropyl)pyridazin-6-one (**10**).

A mixture of **2** (0.5 g, 1.4 mmoles), sodium borohydride (40 mg, 1.1 mmoles), tetrahydrofuran (10 ml) and distilled water (0.2 ml) was stirred for 4 hours at room temperature. After adding acetone (0.5 ml), the reaction mixture was stirred for an additional 1 hour at room temperature. The solvent was evaporated under reduced pressure at room temperature. The resulting residue was applied to a silica gel column (1.5 x 20 cm). The column was eluted with chloroform-methanol (9:1 v/v). The fractions containing the product were combined, and the solvent was evaporated under reduced pressure, the resulting residue was recrystallized from carbon tetrachloride to give compound **10** as a colorless crystal in 82% (0.4 g) yield, mp 59-60°; ir (potassium bromide): 3460, 1684, 1582, 1556 cm^{-1}.

4,5-Dichloro-1-(3-azido-2-hydroxypropyl)pyridazin-6-one (**11**).

A mixture of **3** (1.0 g, 3.8 mmoles), sodium borohydride (0.14 g, 3.7 mmoles), tetrahydrofuran (15 ml) and distilled water (0.7 ml) was stirred for 1 hour at room temperature. After adding acetone (2 ml), the reaction mixture was stirred for an additional 10 minutes. The mixture was dried over anhydrous magnesium sulfate, and the solvent was then evaporated under reduced pressure to give compound **11** as an oil in 99% (0.99 g) yield; ir (neat): 3400, 2940, 2100, 1648, 1580 cm^{-1}.

4,5-Dichloro-1-(2,3-epoxypropyl)pyridazin-6-one (**12**).

After a mixture of **9** (2.0 g, 6.6 mmoles), distilled water (2 ml) and tetrahydrofuran (20 ml) was stirred for 0.5 hour at room temperature, acetone (1 ml) and aqueous potassium hydroxide (10%, 3 ml) were added. The reaction mixture was stirred for 15 minutes at room temperature. The mixture was concentrated to 5 ml under reduced pressure. The product was extracted with chloroform (10 ml x 2). After the chloroform layer was dried over anhydrous magnesium sulfate, the solvent was evaporated under reduced pressure to give compound **12** as an oil in 89% (1.3 g) yield; ir (neat): 3096, 2966, 1670, 1584 cm^{-1}.

4,5-Dichloro-1-(2,3-dihydroxypropyl)pyridazin-6-one (**13**).

A mixture of **12** (0.41 g, 1.85 mmoles), concentrated hydrochloric acid (1 drop) and distilled water (1 ml) was stirred for 5 hours at 40°. The solvent was evaporated under reduced pressure. The product was extracted with ethyl acetate (50 ml x 2). After the ester layer was dried over anhydrous magnesium sulfate, the solvent was evaporated under reduced pressure. The resulting residue was recrystallized from methylene chloride-carbon tetrachloride (1:4 v/v) to give compound **13** as a light yellow crystal in 56% (0.23 g) yield, mp 116-118°; ir (potassium bromide): 3450, 1665, 1584, 963 cm^{-1}.

4,5-Dichloro-1-(2-amino-4-methylthiazol-5-yl)pyridazin-6-one (**14**).

A mixture of **1** (0.60 g, 2 mmoles), thiourea (0.26 g, 3.4 mmoles) and tetrahydrofuran (15 ml) was stirred for 1 hour at 45°. After the solvent was evaporated under reduced pressure, the resulting residue was applied to the top of an open-bed column (1.5 x 10 cm). The column was eluted with chloroform-methanol (9:1 v/v). The fractions containing the product were combined, and the solvent was then evaporated under reduced pressure to give the crude product. The crude product was recrystallized from dichloromethane-carbon tetrachloride (1:2 v/v) to give compound **14** as reddish powder in 54% (0.3 g) yield, mp 140-141° dec; ir (potassium bromide): 3372, 3288, 1652, 1442, 1148 cm^{-1}.

4,5-Dichloro-1-(3-formamidinylthio-2-oxopropyl)pyridazin-6-one (**15**).

A mixture of **1** (0.5 g, 1.7 mmoles), thiourea (0.26 g, 3.4 mmoles) and tetrahydrofuran (8 ml) was stirred for 1 hour at 20° under a nitrogen atmosphere. After the solvent was evaporated under reduced pressure at 20°, the resulting residue was applied to the top of an open-bed column (1.5 x 10 cm). The column was eluted with ethyl acetate. The fractions containing the product were combined, and the solvent was evaporated under reduced pressure at 20°. The crude product was dissolved in a small amount of ethyl acetate, and the solution was then poured into water (50 ml) with stirring. Ethyl acetate was evaporated slowly under ambient pressure at room temperature to produce com-

pound **15** as a yellow powder. The product was filtered and dried in air to give pure **15** in 50% (0.25 g) yield, mp 136° dec; ir (potassium bromide): 3422, 3264, 1660, 1624, 1332 cm^{-1}.

4,5-Dichloro-3-nitro-1-(3-formamidinylthio-2-oxopropyl)pyridazin-6-one (**16**).

A mixture of **2** (0.36 g, 1.04 mmoles), thiourea (0.1 g, 1.3 mmoles) and tetrahydrofuran (10 ml) was stirred for 20 minutes at room temperature. To the above solution, distilled water (50 ml) was added. After tetrahydrofuran was evaporated for 24 hours at room temperature by bubbling air through the solution, the resulting precipitate was filtered off, and washed with distilled water (5 ml x 2) to give compound **16** as yellow crystals. The crude product was dissolved in a small amount of ethyl acetate, and the solution was then poured into water (50 ml) with stirring. Ethyl acetate was evaporated slowly under ambient pressure at room temperature to produce compound **16** as yellow crystals from water. The product was filtered and dried in air to give pure **16** in 54% (0.19 g) yield, mp 167-168° dec; ir (potassium bromide): 3452, 3286, 3092, 1702, 1684, 1530 cm^{-1}.

4,5-Dichloro-1-[(2-aminothiazol-5-yl)methyl]pyridazin-6-one (**17**).

Method A.

A mixture of **1** (300 mg, 1 mmole), thiourea (84 mg, 1.1 mmoles) and ethanol (15 ml) was stirred for 20 minutes at 45°. After the solvent was evaporated under reduced pressure, 10 ml of water was added to the residue with stirring. The resulting precipitate was filtered, and recrystallized from ethanol to give compound **17** as light yellow crystals in 72% (0.2 g) yield, mp 215° dec; ir (potassium bromide): 3400, 3200, 1664, 1620, 1426 cm^{-1}; ms: m/e 277 (M^+).

Method B.

A mixture of **15** (0.37 g, 1 mmole) and ethanol (15 ml) was refluxed for 20 minutes. After the solvent was evaporated under reduced pressure, distilled water (10 ml) was added to the residue with stirring. The resulting precipitate was filtered and recrystallized from ethanol to give compound **17** as light yellow crystals in 72% (0.2 g) yield. Analytical data of this compound was identical with the product from Method A.

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