Journal of the Korean Chemical Society
2014, *Vol. 58, No. 1*
Printed in the Republic of Korea
http://dx.doi.org/10.5012/jkcs.2014.58.1.140

단신 (Notes)

Functionalization of 4,5-Dichloropyridazin-3(2*H*)-one

Gi Hyeon Sung, Bo Ram Kim, Ki Eun Ryu, and Yong-Jin Yoon*
Department of Chemistry & Research Institute of Natural Science, Gyeongsang National University, Jinju 660-701, Korea
**E-mail: yjyoon@gnu.ac.kr*
(Received November 11, 2013; Accepted December 3, 2013)

Key words: Nitration, Formylation, Regioselective substitution

INTRODUCTION

Since the discovery that pyrrolo[2,3-*c*]pyridazine or pyrrolo[2,3-*d*]pyridazine exhibited antiproliferative activity and antiviral activity, much attention has been paid to the development of convenient and efficient routes for synthesis of heterocyclic bases[1,2] such as pyrrolo[2,3-*c*]pyridazine and pyrrolo[2,3-*d*]pyridazine, which are C_4N_2–C_4N type fused ring. In order to modify fused-heterocyclic skeletons for new fungicidal agents, we required C_4N_2–C_3N (pyrrolopyridazine), C_4N_2–C_3N_2 (imidazopyridazine), C_4N_2–C_4N_2 (pyridazinopyridazine or pyridazinopyrimidine) and other type fused rings containing pyridazine moiety. For the synthesis of these fused-heterocyclic bases, 6-nitro and 6-formylpyridazin-3(2*H*)-ones are useful.[3–10] In order to synthesize useful intermediates for some fused pyridazinone and/or new fungicidal agents, we attempted to prepare some 6-nitro-(or amino, hydroxylamino and formyl)pyridazin-3(2*H*)-ones. In this paper, we report the functionalization of 4,5-dichloropyridazin-3(2*H*)-one and 4,5-dichloro-2-methyl-6-nitropyridazin-3(2*H*)-one.

EXPERIMENTAL

General Methods

Melting points were determined with a capillary apparatus and uncorrected. NMR spectra were recorded on a 300 MHz spectrometer (Bruker) with chemical shift values reported in δ units (ppm) relative to an internal standard (TMS). IR spectra were obtained on a Varian 640-IR spectrophotometer. The open-bed chromatography was carried out on silica gel (70–230 mesh, Merck) using gravity flow. The column was packed with slurries. Chemicals were purchased from the Aldrich, TCI or Alfa Aesar chemical company. Compounds **2**[11], **5**[10] and **7**[10] was prepared by the literature methods.

Synthesis of Compounds

4,5-Dichloro-6-nitropyridazin-3(2*H*)-one (3)

A mixture of **2** (32.0 g, 0.19 mol), potassium nitrate (70.0 g, 0.69 mol) and *conc*-sulfuric acid (200 mL) was stirred for 5 hours at 110–120 °C. After cooling to room temperature, the solution was slowly poured into ice-water (400 mL). The resulting yellow crystals was filtered, washed with water (100 mL × 2) and dried in air to give the product. Yield: 32.58 g (80%). yellow crystal. mp 185–186 °C (lit.[6] 184–186 °C); IR (KBr) 1540, 1350 (NO_2) cm^{-1}; ^1H NMR (300MHz, DMSO-d_6) δ 8.06 (bs, 1H, D_2O exchangeable); Anal. Calcd. for $C_4HN_3O_2Cl_2$: C, 22.88; N, 20.01. Found: C, 22.91; N, 20.05.

3,4,5-Trichloro-6-nitropyridazine (4)

A mixture of **3** (2.0 g, 9.53 mmol) and $POCl_3$ (10 mL) was refluxed for 24 hours. After cooling to room temperature, the solution was evaporated under reduced pressure. The resulting residue was slowly poured into ice-water (300 mL). The resulting yellow crystals was filtered, washed with water (100 mL × 2) and dried in air to give the crude product. The crude product was applied on the top of an open-bed silica gel column (3 × 28 cm). The column was eluted with CH_2Cl_2/*n*-hexane (2:1, v/v). Fractions containing the product were combined, evaporated under reduced pressure and dried in air to give compound **4**. Yield: 1.58 g (72%). mp 78 °C; IR (KBr) 1690, 1490 (C=C), 1550, 1350 (NO_2) cm^{-1}; Anal. Calcd. for $C_4N_3O_2Cl_3$: C, 21.03; N, 18.40. Found: C, 21.06; N, 18.48.

4,5-Dichloro-6-formyl-2-methylpyridazin-3(2*H*)-one (6)

After adding of phosphorus oxychloride (5 mL) into a mixture of compound **5** (1.0 g, 5.59 mmol) and DMF (8 mL) at room temperature, the reaction mixture was stirred for 12 hours at 80–90 °C. The mixture was cooled to room temperature, and then poured into cold sodium acetate

solution (water 200 mL and NaOAc 5.0 g) with stirring. The product was extracted with CH_2Cl_2 (50 mL × 3). The organic layer was separated and dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure, and the resulting residue was applied to the top of an open-bed silica gel column (2.6 × 20 cm). The column was eluted with CH_2Cl_2/*n*-hexane (1:1, v/v). Fractions containing the product were combined, and evaporated under reduced pressure to give compound **6**. Yield: 0.91 g (78%). white crystal. mp 93 °C; IR (KBr) 2850 (aldehyde C–H), 1740 (C=O) cm^{-1}; ^1H NMR (300MHz, DMSO-d_6) δ 9.51 (s, 1H), 3.35 (s, 3H). Anal. Calcd. for $C_6H_4N_2O_2Cl_2$: C, 34.81; H, 1.95; N, 13.53. Found: C, 34.85; H, 1.99; N, 13.58.

6-Amino-4,5-dichloro-2-methylpyridazin-3(2*H*)-one (8)

A mixture of **7** (3.0 g, 13.39 mmol), $NaBH_4$ (0.98 g, 26.78 mmol), $SnCl_2·2H_2O$ (5.87 g, 26.78 mmol) and chloroform (30 mL) was stirred for 24 hours at room temperature. The mixture was filtered and washed with chloroform (30 mL). The resulting solution was concentrated to 20 mL. The residue was applied to the top of an open-bed silica gel column (2.7 × 28 cm). The column was eluted with chloroform. Fractions containing the product were combined, evaporated under reduced pressure and dried in air to give the compound **8**. Yield: 2.08 g (80%). mp 191–193 °C (lit.[10] mp 193–195 °C); IR (KBr) 3450, 3350, 3250 (tautomeric NH_2), 1675 (C=O) cm^{-1}; ^1H NMR (300MHz, DMSO-d_6): δ 9.00 (bs, 1H, D_2O exchangeable), 8.64 (s, 1H, D_2O exchangeable), 6.20 (s, 2H, D_2O exchangeable), 3.51 (s, 3H); Anal. Calcd. for $C_5H_5N_3OCl_2$: C, 30.95; H, 2.60; N, 21.66. Found: C, 30.98; H, 2.65; N, 21.70.

4,5-Dichloro-6-hydroxyamino-2-methylpyridazin-3(2*H*)-one (10)

A mixture of **7** (2.0 g, 8.93 mmol), acetic acid (15 mL) and zinc-dust (0.54 g) was stirred for 23 hours at room temperature. The reaction mixture was poured into ice water (200 mL) with stirring. The resulting crystals were filtered, washed with water (200 mL) and dried in air to give the crude product. The crude product was applied to the top of an open-bed silica gel column (2.5 × 30 cm). The column was eluted with chloroform. Fractions containing the product were combined, evaporated under reduced pressure and dried in air to give compound **10**. Yield: 1.31 g (70%). mp 219–220 °C; IR (KBr) 3450 (OH), 3350 (NH), 1675 (C=O) cm^{-1}; ^1H NMR (300MHz, $CDCl_3$) δ 6.70 (bs, 1H, D_2O exchangeable), 4.60 (bs, 1H, D_2O exchangeable), 3.90 (s, 3H); Anal. Calcd. for $C_5H_5N_3O_2Cl_2$: C, 28.59; H, 2.40; N, 20.01. Found: C, 28.62; H, 2.44; N, 20.05.

4-Chloro-5-cyano-2-methyl-6-nitropyridazin-3(2*H*)-one (11a)

A mixture of **7** (3.0 g, 13.39 mmol), cuprous cyanide (1.29 g, 14.46 mmol) and dimethyl sulfoxide (30 mL) was stirred for 20 hours at 90–100 °C. After cooling to room temperature, the mixture was poured into ice water (1.0 L) with stirring. The resulting crystals were filtered, washed with cold water (500 mL) and dried in air to give **11a**. Yield: 2.30 g (80%). mp 260 °C; IR (KBr) 2400 (CN), 1675 (C=O), 1500, 1350 (NO_2) cm^{-1}; ^1H NMR (300MHz, DMSO-d_6) δ 3.40 (s, 3H); Anal. Calcd. for $C_6H_3N_4O_3Cl$: C, 33.59; H, 1.41; N, 26.11. Found: C, 33.62; H, 1.45; N, 26.14.

4-Chloro-2-methyl-5,6-dinitropyridazin-3(2*H*)-one (11b)

Compound **7** (2.0 g, 8.93 mmol) was dissolved in methanol (50 mL). Sodium nitrite solution ($NaNO_2$, 1.36 g, 16.0 mmol in 10 mL water) was slowly added to above solution. The mixture was refluxed for 10 minutes. After cooling to room temperature, the mixture was stirred for 24 hours at room temperature. The reaction mixture was filtered and washed with methanol (20 mL). The combined filtrate was evaporated under reduced pressure. The resulting residue was applied to the top of an open-bed silica gel column (2.5 × 26 cm). The column was eluted with chloroform (100 mL) and then ethyl acetate. Fractions containing the product were combined, evaporated under reduced pressure to give compound **11b**. Yield: 1.57 g (75%). mp 262 °C (decomposed); IR (KBr) 1660 (C=O), 1570, 1350 (NO_2) cm^{-1}; ^1H NMR (300MHz, DMSO-d_6) δ 3.45 (s, CH_3); Anal. Calcd. for $C_5H_3N_4O_5Cl$: C, 25.60; H, 1.29; N, 23.89. Found: C, 25.63; H, 1.32; N, 23.91.

4-Chloro-5-hydroxyamino-2-methyl-6-nitropyridazin-3(2*H*)-one (11c)

Hydroxylamine hydrochloride (0.74 g, 10.71 mmol) and sodium acetate (0.88 g, 10.71 mmol) was dissolved in ethanol (35 mL). After a solution of **7** (2.0 g, 8.93 mmol in EtOH / EtOAc (15 mL, 2:1, v/v)) was slowly added to above mixture, potassium carbonate (1.48 g, 10.71 mmol) was added. The reaction mixture was stirred for 24 hours at room temperature. After the reaction mixture was filtered, the resulting filtrate was evaporated with silica gel (1.5 g) under reduced pressure. The resulting residue was applied to the top of an open-bed silica gel column (3 × 33 cm). The column was eluted with ethyl acetate. Fractions containing the product were combined, evaporated under reduced pressure to give compound **11c**. Yield: 1.58g (80%). mp 183–

184 °C; IR (KBr) 3490, 3350 (OHNH), 1675 (C=O), 1510, 1350 (NO_2) cm^{-1}; ^1H NMR (300MHz, DMSO-d_6) δ 6.00 (bs, 1H, D_2O exchangeable), 5.80 (bs, 1H, D_2O exchangeable), 3.68 (s, 3H); Anal. Calcd. for $C_5H_5N_4O_4Cl$: C, 27.23; H, 2.28; N, 25.40. Found: C, 27.26; H, 2.32; N, 25.45.

4-Chloro-2-methyl-5-methylamino-6-nitropyridazin-3(2*H*)-one (11d)

A mixture of **7** (2 g, 8.93 mmol), sodium acetate (1.68 g, 20.53 mmol), methylamine hydrochloride (0.72 g, 10.71 mmol) and methanol (35 mL) was stirred for 30 hours at room temperature. After the reaction mixture was filtered, the resulting filtrate was evaporated under reduced pressure. The resulting residue was applied to the top of an open-bed silica gel column (2.6 × 30 cm). The column was eluted with chloroform. Fractions containing the product were combined, evaporated under reduced pressure to give compound **11d**. Yield: 1.50 g (77%). reddish yellow crystals. mp 150–152 °C; IR (KBr) 3350 (NH), 1675 (C=O), 1550, 1350 (NO_2) cm^{-1}; ^1H NMR (300MHz, DMSO-d_6) δ 7.11 (bs, 1H, D_2O exchangeable), 3.65 (s, 3H), 3.28 (d, 3H, J = 3.0 Hz); Anal. Calcd. for $C_6H_7N_4O_3Cl$: C, 32.97; H, 3.23; N, 25.63. Found: C, 33.01; H, 3.27; N, 25.66.

4-Chloro-2-methyl-5-[*N*-(2,4-dinitrophenyl)hydrazino]-6-nitropyridazin-3(2*H*)-one (11e)

Compound **7** (1.0 g, 4.46 mmol) was dissolved in absolute methanol (40 mL). Methanolic hydrazine solution (2,4-dinitrophenylhydrazizne hydrochloride, 1.06 g, 5.35 mmol and triethyl amine 0.947 mL in absolute methanol 10 mL) was slowly added to above solution. The reaction mixture was stirred for 24 hours at room temperature. After the reaction mixture was filtered, the resulting filtrate was evaporated under reduced pressure. The resulting residue was applied to the top of an open-bed silica gel column (2.8 × 30 cm). The column was eluted with *n*-hexane/chloroform (10:3, v/v). Fractions containing the product were combined, evaporated under reduced pressure to give compound **11e**. Yield: 1.38 g (80%). mp 172–173 °C; IR (KBr) 3350 (NH), 1715 (C=O), 1550, 1350 (NO_2) cm^{-1}; ^1H NMR (300MHz, DMSO-d_6) δ 10.76 (bs, 2H, D_2O exchangeable), 8.81 (s, 1H), 8.32 (d, 1H, J = 9.5 Hz), 7.75 (d, 1H, J = 9.5 Hz), 2.1 (s, 3H); Anal. Calcd. for $C_{11}H_8N_7O_7Cl$: C, 34.26; H, 2.09; N, 25.42. Found: C, 34.30; H, 2.12; N, 25.45.

4-Chloro-2-methyl-5-(2-nitrophenyl)amino-6-nitropyridazin-3(2*H*)-one (11f)

A mixture of **7** (1.0 g, 4.46 mmol), triethylamine (0.93 mL, 6.69 mmol), *o*-nitroaniline (0.74 g, 5.36 mmol) was dissolved in absolute methanol (20 mL). The reaction mixture was stirred for 23 hours at room temperature. After the reaction mixture was filtered, the resulting filtrate was evaporated under reduced pressure. The resulting residue was applied to the top of an open-bed silica gel column (2.5 × 30 cm). The column eluted with *n*-hexane/chloroform (10:4, v/v). Fractions containing the product were combined, evaporated under reduced pressure to give compound **11f**. Yield: 1.16 g (80%). mp 62 °C; IR (KBr) 3350 (NH), 1650 (C=O), 1550, 1350 (NO_2) cm^{-1}; ^1H NMR (300MHz, DMSO-d_6) δ 7.38 (bs, 1H, D_2O exchangeable), 7.94 (t, 1H, J = 8.8 Hz), 7.40–7.30 (m, 1H), 7.00 (t, 1H, J_1 = 8.8 Hz, J_2 = 8.3 Hz), 6.63–6.50 (m, 1H), 3.41 (s, 3H); Anal. Calcd. for $C_{11}H_8N_5O_5Cl$: C, 40.57; H, 2.48; N, 21.50. Found: C, 40.60; H, 2.50; N, 21.53.

4-Chloro-2-methyl-5-(4-nitrophenyl)amino-6-nitropyridazin-3(2*H*)-one (11g)

A mixture of **7** (1.0 g, 4.46 mmol), triethylamine (0.93 mL, 6.69 mmol), *p*-nitroaniline (1.23 g, 8.93 mmol) was dissolved in absolute methanol (20 mL). The reaction mixture was stirred for 16 hours at 88–90 °C. After cooling to room temperature and then filtered, the resulting filtrate was evaporated under reduced pressure. The resulting residue was applied to the top of an open-bed silica gel column (2.5 × 30 cm). The column eluted with *n*-hexane/chloroform (8:5, v/v). Fractions containing the product were combined, evaporated under reduced pressure to give compound **11g**. Yield: 1.16 g (80%). mp 140 °C; IR (KBr) 3250 (NH), 1710 (C=O), 1500, 1310 (NO_2) cm^{-1}; ^1H NMR (300MHz, DMSO-d_6) δ 7.94 (t, 1H, J = 11.6 Hz), 6.70 (bs, 1H, D_2O exchangeable), 6.60 (d, 1H, J = 7.3 Hz), 4.1 (s, 3H); Anal. Calcd. for $C_{11}H_8N_5O_5Cl$: C, 40.57; H, 2.48; N, 21.50. Found: C, 40.61; H, 2.50; N, 21.54.

5-(Benzo[*d*]thiazol-2-yl)thio-4-chloro-2-methyl-6-nitropyridazin-3(2*H*)-one (11h)

A mixture of 2-mercaptobenzothiazole (0.895 g, 5.54 mmol), KOH (0.38 g, 6.69 mmol), **7** (1.0 g, 4.46 mmol) was dissolved in THF (30 mL). The reaction mixture was stirred for 19 hours at room temperature. After the reaction mixture was filtered, the resulting filtrate was evaporated with silica gel (1.5 g) under reduced pressure. The resulting residue was applied to the top of an open-bed silica gel column (2.6 × 28 cm). The column was eluted with CCl_4/EtOAc (8:1, v/v). Fractions containing the product were combined, evaporated under reduced pressure to give compound **11h**. Yield: 1.31 g (83%). mp 140–142 °C; IR (KBr)

1680 (C=O), 1570, 1375 (NO_2) cm^{-1}; ^1H NMR (300MHz, DMSO-d_6) δ 8.70–8.68 (m, 2H), 7.51–7.18 (m, 2H), 3.68 (s, 3H); Anal. Calcd. for $C_{12}H_7N_4O_3S_2Cl$: C, 40.62; H, 1.99; N, 15.79. Found: C, 40.61; H, 2.02; N, 15.82.

4-Chloro-2-methyl-6-nitro-5-(pyrimidin-2-yl)thiopyridazin-3(2*H*)-one (11i)

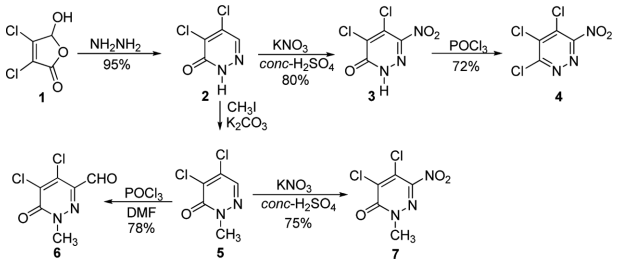
A mixture of 2-mercaptobenzothiazole (0.6 g, 5.35 mmol), KOH (0.38 g, 6.69 mmol), **7** (1.0 g, 4.46 mmol) was dissolved in THF (30 mL). The reaction mixture was stirred for 22 hours at room temperature. After the reaction mixture was filtered, the resulting filtrate was evaporated with silica gel (1.5 g) under reduced pressure. The resulting residue was applied to the top of an open-bed silica gel column (2.6 × 28 cm). The column was eluted with chloroform. Fractions containing the product were combined, evaporated under reduced pressure to give compound **11i**. Yield: 1.07 g (80%). mp 72 °C; IR (KBr) 1675 (C=O), 1550, 1340 (NO_2) cm^{-1}; ^1H NMR (300MHz, DMSO-d_6) δ 8.43–8.35 (m, 2H), 7.10–6.92 (m, 1H), 3.68 (s, 3H); Anal. Calcd. for $C_9H_6N_5O_3SCl$: C, 36.07; H, 2.02; N, 23.37. Found: C, 36.12; H, 2.05; N, 23.41.

4-Chloro-5-(dicyanomethyl)-2-methyl-6-nitropyridazin-3(2*H*)-one (11j)

Malononitrile (0.663 g, 10.04 mmol) was treated with NaH (0.67 g, 16.74 mmol, 60% in oil) in THF (25 mL). The reaction mixture was stirred for 30 minute at room temperature. Tetrahydrofuran solution of **7** (1.5 g, 6.69 mmol in 25 mL THF) was slowly added to above solution with stirring. The reaction mixture was refluxed for 18 hours. After cooling to room temperature, the mixture was filtered. The resulting filtrate was evaporated with silica gel (1.0 g) under reduced pressure. The resulting residue was applied to the top of an open-bed silica gel column (3 × 40 cm). The column was eluted with EtOH / EtOAc (1:19, v/v). Fractions containing the product were combined, evaporated under reduced pressure to give **11j**. Yield: 1.49 g (88%). mp 212 °C; IR (KBr) 2200 (CN), 1675 (C=O), 1550, 1350 (NO_2) cm^{-1}; ^1H NMR (300MHz, DMSO-d_6) δ 3.60 (s, 1H), 3.50 (s, 3H); Anal. Calcd. for $C_8H_4N_5O_3Cl$: C, 37.89; H, 1.59; N, 27.62. Found: C, 37.92; H, 1.63; N, 27.67.

RESULTS AND DISCUSSION

Nitration of 4,5-dichloropyridazin-3(2*H*)-one (**2**)[11] with potassium nitrate and *conc*-sulfuric acid gave 4,5-dichloro-6-nitropyridazin-3(2*H*)-one (**3**) in 80% yield, whereas compound **2** was reacted with potassium nitrate and fuming

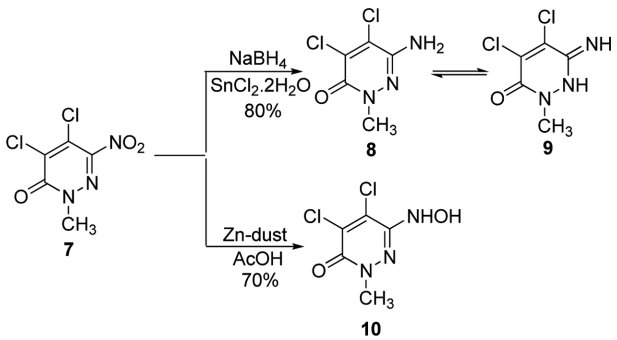


***Scheme* 1.** Functionalization of 4,5-dichloropyridazin-3(2*H*)-one.

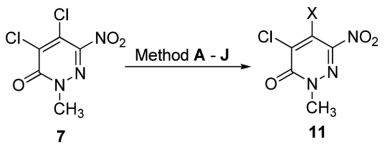
sulfuric acid instead of *conc*-sulfuric acid to afford compound **3** in low yield. Chlorination of compound **3** with phosphorus oxychloride also gave 3,4,5-trichloro-6-nitropyridazine (**4**) in 72% yield. Compound **5** was prepared from **2** by the literature method.[12] Nitration of **5** with potassium nitrate and *conc*-sulfuric acid gave 4,5-dichloro-2-methyl-6-nitropyridazin-3(2*H*)-one (**7**) in 75% yield. Compound **5** was also treated with $POCl_3$ and DMF to afford **6** in 78% yield.

On the other hand, we reported the reduction of **7** with Fe/NH_4Cl.[10] Although the yield of this method is high, we required a novel reduction system because that a trace iron is interrupted during screening of biological activity. Therefore, we attempted to reduce compound **7** using sodium borohydride. Reduction of **7** with $NaBH_4/SnCl_2{\cdot}2H_2O$ in chloroform afforded 6-amino-4,5-dichloro-2-methylpyridazin-3(2*H*)-one (**8**) in 80% yield. In the spectrum of IR for **8**, three absorption peaks of NH showed at 3450, 3350 and 3250 cm^{-1}. Three proton signals were also detected at δ 9.0 (1H), 8.64 (1H) and 6.20 (2H) ppm in the spectrum of ^1H NMR for **8**. These are due to two tautomers **8** and **9**. On the other hand, compound **7** was treated with zinc-dust in acetic acid to give 4,5-dichloro-6-hydroxyamino-2-methylpyridazin-3(2*H*)-one (**10**) in 70% yield.

In addition, we attempted to synthesize 4-chloro-2-methyl-6-nitropyridazin-3(2*H*)-one derivatives.[11] Cyanation of compound **7** with CuCN in dimethylsulfoxide afforded the



***Scheme* 2.** Reduction of compound **7**.



Method **A**: CuCN, DMSO Method **B**: $NaNO_2$, MeOH/H_2O
Mehtod **C**: $NH_2OH.HCl$, NaOAc, EtOH Method **D**: $NH_2Me.HCl$, NaOAc, MeOH
Method **E**: 2,4-$(NO_2)_2PhNHNH_2$ HCl, Et_3N, MeOH(dry)
Method **F**: *o*-nitroaniline, Et_3N, MeOH(dry) Method **G**: *p*-nitroaniline, Et_3N, MeOH(dry)
Method **H**: 2-mercaptobenzothiazole, KOH, THF Method **I**: 2-mercaptopyrimidine, KOH, THF
Method **J**: malononitrile, NaH, THF

11	**a**	**b**	**c**	**d**	**e**	**f**
X	CN	NO_2	NHOH	NHMe	HNHN-(2,4-$(NO_2)_2$Ph)	HN-(2-NO_2Ph)
Method	A	B	C	D	E	F
Yield(%)	80	75	80	77	80	80

11	**g**	**h**	**i**	**j**
X	HN-(4-NO_2Ph)	2-benzothiazolyl-S	2-pyrimidinyl-S	$CH(CN)_2$
Method	G	H	I	J
Yield(%)	80	83	80	88

***Scheme* 3.** Functionalization of compound **7**.

corresponding 5-cyano derivative **11a** in 80% yield. Compound **7** was treated with sodium nitrite in methanol-water to give the corresponding 5,6-dinitropyridazin-3(2*H*)-one **11b** in 75% yield. Treatment of **7** with NH_2OH·HCl or $NHCH_3$·HCl in the presence of sodium acetate in ethanol or methanol afforded the corresponding 5-hydroxyamino (**11c**, 80%) or 5-methylamino (**11d**, 77%) derivatives. Compound **7** was also treated with 2,4-dinitrophenylhydrazine hydrochloride in the presence of triethylamine in methanol (dry) to give 4-chloro-6-nitro-5-(dinitrophenylhydrazino)-2-methylpyridazin-3(2*H*)-one (**11e**) in 80% yield. Reaction of **7** with *o*-nitroaniline or *p*-nitroaniline in the presence of triethylamine in methanol (dry) afforded the corresponding 5-anilino derivatives **11f** or **11g** in 80% yields, respectively.

On the other hand, we attempted to introduce ArS-moiety at C-5. Treatment of **7** with 2-mercaptobenzotriazole or 2-mercaptopyrimidine in the presence of KOH in THF to give the corresponding 5-ArS-derivatives **11h** (83%) or **11i** (80%). We also attempted to synthesize 5-(dicyano)methyl deriveative as the intermediate of C_4N_2–C_4N (or C_4N_2–C_4N–C_4N) fused bicyclic (or tricyclic) ring. Treatment of **7** with malononitrile in the presence of NaH in THF (dry) gave 4-chloro-5-(dicyano)methyl-6-nitropyridazin-3(2*H*)-one (**11j**) in 82% yield. The structures of all synthetic compounds were established by IR, ^{1}H NMR and elemental analysis. The regiochemistry of the substituents was confirmed by further reactions such as synthesis of fused ring or other derivatives.

CONCLUSION

In conclusion, we regioselectively synthesized twelve 4-chloro-5-substituted-6-nitropyridazin-3(2*H*)-ones involving amino, hydoxylamino, nitro, cyano and arylthio groups from 4,5-dichloropyridazin-3(2*H*)-one via two and/or three steps. It is worthy to note that our methods are regioselective, easy and good yields although compounds **2**, **3**, **5** and **7** involve two or three electrophilic reaction site.

Further work including the chemical transformation, the synthesis of fused ring and fungicidal activity is under way in our laboratory.

Acknowledgments. This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2012RIAIA2001162).

REFERENCES

1. Renau, T. E.; Wotring, L. L.; Drach, J. C.; Townsend, L. B. *J. Med. Chem*. **1996**, *39*, 873.
2. Renau, T. E.; Kennedy, C.; Park, R. G.; Breitenbach, J. M.; Drach, J. C.; Townsend, L. B. *J. Med. Chem*. **1996**, *39*, 3470.
3. Lee, S. G.; Choi, S. Y.; Yoon, Y. J. *J. Heterocyclic Chem*. **1992**, *29*, 1409.
4. Park, J. W.; Kweon, D. H.; Kang, Y. J.; Lee, W. S.; Cho, S. D.; Yoon, Y. J. *J. Heterocyclic Chem*. **2000**, *37*, 5.
5. Lee, S. G.; Kweon, D. H.; Yoon, Y. J. *J. Heterocyclic Chem*. **2001**, *38*, 1179.
6. Katz, D. J.; Wise, D. S.; Townsend, L. B. *J. Heterocyclic Chem*. **1983**, *20*, 369.
7. Choi, S. Y.; Lee, S. G.; Yoon, Y. J. *J. Heterocyclic Chem*. **1991**, *28*, 1235.
8. Choi, S. Y.; Shin, S. C.; Yoon, Y. J. *J. Heterocyclic Chem*. **1991**, *28*, 385.
9. Choi, W. Y.; Cho, S. D.; Kim, S. K.; Yoon, Y. J. *J. Heterocyclic Chem*. **1997**, *34*, 1307.
10. Kweon, D. H.; Cho, S. D.; Kim, S. K.; Chung, J. W.; Yoon, Y. J. *J. Heterocyclic Chem*. **1996**, *33*, 1915.
11. Mowry, D. T. *J. Am. Chem. Soc*. **1953**, *75*, 1909.
12. Cho, S. D.; Choi, W. Y.; Yoon, Y. J. *J. Heterocyclic Chem*. **1996**, *33*, 1579.