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NUCLEOPHILIC SUBSTITUTION REACTIONS OF 4,5-DICHLORO-2-METHYL-6-NITRO-*2H*-PYRIDAZIN-3-ONE

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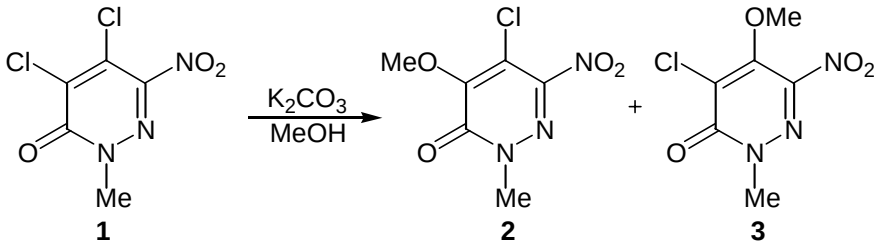
Abstract-4,5-Dichloro-2-methyl-6-nitro-*2H*-pyridazin-3-one (**1**) reacts with various substituted phenols and 2-mercaptopyrimidine in the presence of NaH or K_2CO_3 to give 3(*2H*)-pyridazinones (**4**, **5a-9a**, **5b-9b**, and **7c**) in high yields. The regiochemistry was confirmed by X-Ray analysis and nOe experiments.

Since the discovery that pyrrolo[2,3-*d*]pyrimidine or pyrrolo[2,3-*c*]pyridazine exhibited antiproliferative activity and/or antiviral activity, much attention has been paid to the development of convenient and efficient routes for synthesis of heterocyclic bases.[1] As a modification of heterocyclic base, we reported recently the results for the synthesis of new *N*-acyclonucleosides containing pyrrolo[2,3-*c*]pyridazine skeleton utilizing 4,5-dichloro-2-methyl-6-nitro-*2H*-pyridazin-3-one (**1**).[2] Then, the nitro group at 6-position of compound (**1**) is essential for the synthesis of fused-heterocycles containing pyridazinone and various trisubstituted pyridazin-3-ones. In connection with nucleophilic substitution reaction of halogens using various trisubstituted pyridazin-3-ones,[3] we reported that the methoxylation of compound (**1**) under the K_2CO_3/MeOH system gave 4-methoxylated pyridazinone (**2**) as a major product and 5-methoxylated pyridazinone (**3**) as a minor product in 62 and 28% yields, respectively (Scheme 1).[4] In order to examine the substitution reaction toward nucleophiles and further synthetic application, we investigated in detail the substitution reaction of 4,5-dichloro-2-methyl-6-nitro-*2H*-pyridazin-3-one (**1**) with various substituted phenols and mercaptopyrimidine in the presence of NaH or K_2CO_3.

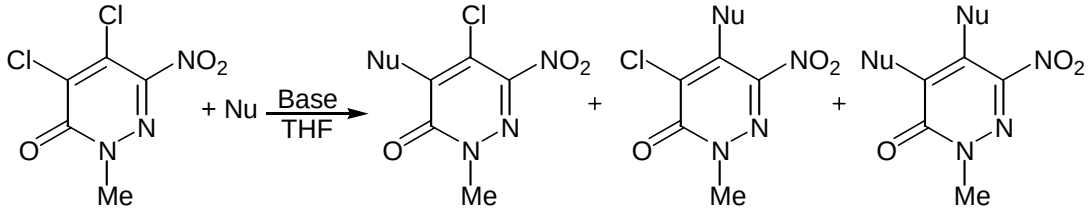


Scheme 1

The requisite compound (**1**) was prepared by Yoon's method,[2] namely, nitration of 4,5-dichloro-2-methyl-*2H*-pyridazin-3-one with potassium nitrate and concentrated sulfuric acid gave 4,5-dichloro-2-methyl-6-nitro-*2H*-pyridazin-3-one (**1**) in 82% yield. Subsequently, we investigated nucleophilic substitution of halogen of compound (**1**) utilizing phenoxide or mercaptopyrimidine sulfone anion which was prepared by treatment of various substituted phenols or mercaptopyrimidine with a base NaH or K_2CO_3. The results are summarized in Table 1. Interestingly, compound (**1**) regioselectively reacted with *p*-methoxyphenol in the presence of NaH at 0 ºC to give the 5-chloro-4-(4-methoxyphenoxy)-2-methyl-6-nitro-*2H*-pyridazin-3-one (**4**) as the sole product in a good yield (Run 1). Compound (**1**) was treated with phenol (or *p*-chlorophenol) and NaH in THF to produce the corresponding compounds (**5a**) (56%), (**5b**) (16%), (**6a**) (74%), and (**6b**) (15%), respectively (Runs 4 and 6). Similar treatment of **1** with *p*-cyanophenol and NaH gave compounds (**7a**) (48%), (**7b**) (24%), and 4,5-bis(4-cyanophenoxy)-2-methyl-6-nitro-*2H*-pyridazin-3-one (**7c**) (8%) (Run 8). The reaction of **1** with *p*-nitrophenol proceeded under the mild conditions to furnish the corresponding **8a** (55%) and **8b** (17%) (Run 10). Tentatively, compound (**1**) was treated with mercaptopyrimidine to afford the corresponding **9a** (60%) and **9b** (29%) (Run 12) (*Method A*).

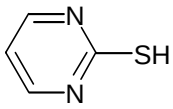
On the other hand, we attempted the nucleophilic substitution of compound (**1**) under the refluxing condition using K_2CO_3. The results are summarized in Table 1. Namely, compound (**1**) reacted with *p*-methoxyphenol to give only 5-chloro-4-(4-methoxyphenoxy)-2-methyl-6-nitro-*2H*-pyridazin-3-one (**4**) in 97% yield (Run 2) (*Method B*), whereas this reaction did not proceed when used $AgNO_3$ (Run 3). According to *Method B,* compound (**1**) was subjected to various nucleophilic substitutions to give the corresponding **5a-9a, 5b-9b,** and **7c** in high yields, respectively (Runs 5, 7, 9, 11, and 13). Although the regioselectivity in these reactions employing K_2CO_3 is not variable, the yield was much higher than that using NaH. In general, nucleophilic substitution of halogens of the heterocycles using potassium alkoxide anion has been proven to be a conventional method for the chemical manipulation of heterocycles.[3] More recently, Lemière group[5] reported that palladium-catalyzed amination on 4-chloro-3(*2H*)-pyridazinones, while using an excess of K_2CO_3 as a base, could be a general and efficient approach to different aryl- and

heteroarylaminopyridazinones. However, it is of some limited use for the multihalogens-substituted pyridazinones because it seems to be difficult to obtain the product selectively.

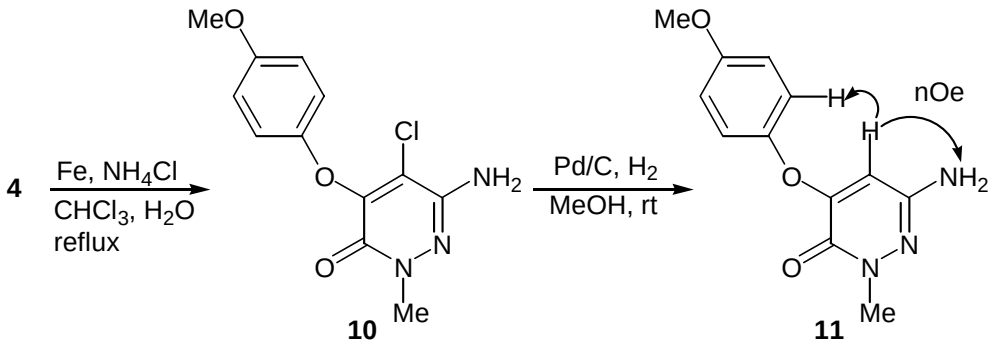


1 **4, 5a-9a** **5b-9b** **7c**

Table 1. Nucleophilic substitution using 4,5-dichloro-2-methyl-6-nitropyridazin-3-one

Run	Nucleophile	Base[a]	Temp	Time	Yield (%) of **4,5a-9a**[b]	Yield (%) of **5b-9b**[b]	Yield (%) of **7c**[b]
1	*p*-$MeOC_6H_4OH$	N	0 °C	25 min	**4** (70)	none	
2	"	K	reflux	6 h	**4** (97)	"	
3	"	A	"	7 h	none	"	
4	PhOH	N	0 °C	20 min	**5a** (56)	**5b** (16)	
5	"	K	reflux	24 h	**5a** (80)	**5b** (19)	
6	*p*-ClC_6H_4OH	N	0 °C	20 min	**6a** (74)	**6b** (15)	
7	"	K	reflux	8 h	**6a** (72)	**6b** (20)	
8	*p*-CNC_6H_4OH	N	rt	2 h	**7a** (48)	**7b** (24)	**7c** (8)
9	"	K	reflux	16 h	**7a** (60)	**7b** (22)	**7c** (14)
10	*p*-$NO_2C_6H_4OH$	N	rt	3 h	**8a** (55)	**8b** (17)	
11	"	K	"	4 h	**8a** (60)	**8b** (33)	
12		N	0 °C	1 h	**9a** (60)	**9b** (29)	
13	"	K	rt	3 h	**9a** (67)	**9b** (25)	

a) Base: N = NaH, K = K_2CO_3, A = $AgNO_3$. b) Isolated yields.

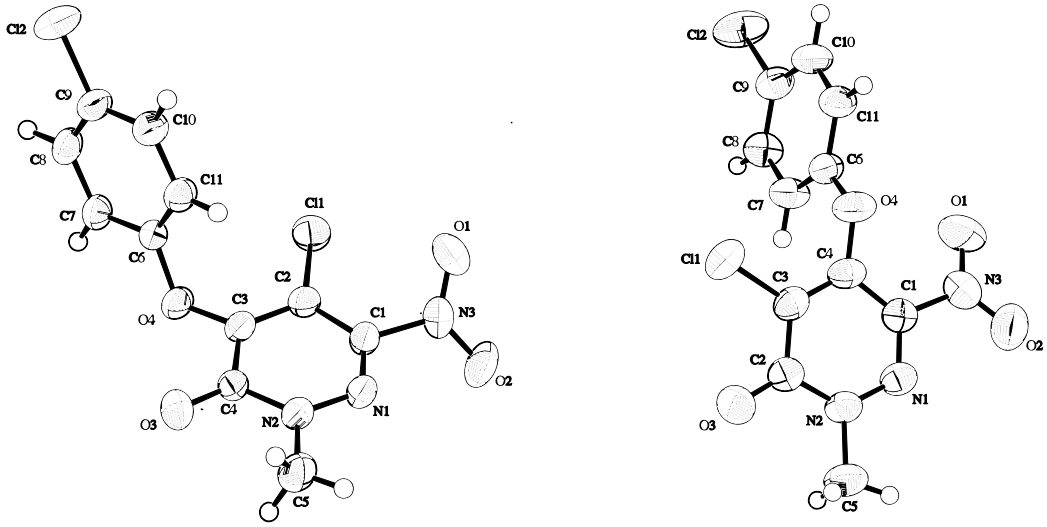


10 **11**

Scheme 2

In order to determine the position of *p*-methoxyphenoxy group on **4**, reduction of compound (**4**) with iron/ammonium chloride/chloroform/water system[6] afforded the corresponding 6-amino-5-chloro-4-(4-

methoxyphenoxy)-2-methyl-*2H*-pyridazin-3-one (**10**). Compound (**10**) was dehalogenated with Pd/C under hydrogen atmosphere to give 6-amino-4-(4-methoxyphenoxy)-2-methyl-*2H*-pyridazin-3-one (**11**) in 80% yield. Then, the position of the *p*-methoxyphenoxy group for **4** was established by the nOe [between C5-H proton and C6-NH_2 protons (or phenyl protons)] experiments (Scheme 2). The structures of *2H*-pyridazin-3-ones (**4, 5a-9a, 5b-9b,** and **7c**) were confirmed on the basis of their characteristic spectroscopic data. Also, the substituted position of the *p*-chlorophenol group on **6a** and **6b** was easily established by X-Ray crystallographic analysis (Figure 1).[7]



6a **6b**

Figure 1 X-Ray crystal structures of **6a** and **6b**.

On the basis of the X-Ray representation or ortep drawing of **6a** and **6b**, the ^{1}H-NMR spectra of all products showed that the chemical shift values of 2-CH_3 group [each singlet for (δ 3.69-3.83 ppm) **4, 5a-9a**] are lower than those of 2-CH_3 group [each singlet for (δ 3.80-3.98 ppm) **5b-9b**]. The ^{13}C-NMR spectra also show carbon signals of 2-CH_3 group in a range of δ 40.2-41.2 ppm for **4, 5a-9a**, whereas δ 41.2-44.2 ppm for **5b-9b**. The chemical behavior of these compounds is also agreement with the assigned structure; namely, 4-substituted *2H*-pyridazin-3-ones (**4, 5a-9a**) show a strong band in a range of 1665-1685 cm^{-1} due to attributed to the amide group, whereas 1669-1688 cm^{-1} for compounds (**5b-9b**).

In conclusion, the nucleophilic substitution of halogens of **1** with various substituted phenols or 2-mercaptopyrimidine has been achieved. All compounds obtained should be useful for synthesis of heterocyclic bases in the nucleoside or acyclonucleoside chemistry.

EXPERIMENTAL

Melting points were determined with a Thomas-Hoover capillary apparatus and are uncorrected. NMR spectra were obtained on a Bruker FTNMR-DRX 500 spectrometer with chemical shift values reported in units (part per million) relative to an internal standard (tetramethylsilane). IR spectral data were obtained on a Hitachi 270-50 spectrophotometer. Elemental analyses were performed with Perkin Elmer 240C. X-Ray diffraction data were obtained with a Rigaku AFC7R diffractometer with filtered Cu-Kα radiation and a rotating anode generator. Open chromatography was carried out with silica gel 60 (70-230 mesh, Merck). The column was packed as slurries with the elution solvent.

Reaction of 1 with methoxyphenol

General procedures

The reaction was carried out in two different experimental conditions.

5-Chloro-4-(4-methoxyphenoxy)-2-methyl-6-nitro-*2H*-pyridazin-3-one (4)

Method A: To a suspension solution of NaH (60% in mineral oil, 71.6 mg, 1.79 mmol) in THF (10 mL) was added a solution of *p*-methoxyphenol (222.2 mg, 1.79 mmol) in 5 mL of THF at 0 ºC. After being stirred for 25 min, the solution of **1** (400 mg, 1.79 mmol) in THF (10 mL) was added slowly. After 25 min, the reaction mixture was quenched by addition of 5% HCl and then extracted with CH_2Cl_2. The combined organic layer was washed with a saturated aqueous $NaHCO_3$ solution, brine, and dried over anhydrous $MgSO_4$. Filtration and evaporation gave a residue, which was purified by column chromatography on silica gel (EtOAc : hexane = 1 : 2) to give 5-chloro-4-(4-methoxyphenoxy)-2-methyl-6-nitro-*2H*-pyridazin-3-one (**4**) (557.9 mg, 70%) as pale yellow prisms, mp 86-88 ºC (CH_2Cl_2/hexane); IR (KBr) 3019, 2970, 1681, 1579, 1499 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.69 (s, 3H), 3.71 (s, 3H), 6.86 (d, *J* = 7.0 Hz, 2H), 6.95 (d, *J* = 7.0 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 40.9, 56.1, 115.1, 115.4, 118.6, 120.2, 149.3, 150.6, 155.6, 157.1. Anal. Calcd for $C_{12}H_{10}N_3O_5Cl$: C, 46.24; H, 3.23; N, 13.48. Found: C, 46.39; H, 3.02; N, 13.25.

Method B: A mixture of **1** (400 mg, 1.79 mmol), K_2CO_3 (62.2 mg, 1.79 mmol) and *p*-methoxyphenol (222.2 mg, 1.79 mmol) in 10 mL of THF was refluxed for 6 h. After cooling to rt, the reaction mixture was quenched by addition of 5% HCl and then extracted with CH_2Cl_2. The combined organic layer was washed with a saturated aqueous $NaHCO_3$ solution, brine, and dried over anhydrous $MgSO_4$. Filtration and evaporation gave a residue, which was purified by column chromatography on silica gel (EtOAc : hexane = 1 : 2) to give 5-chloro-4-(4-methoxyphenoxy)-2-methyl-6-nitro-*2H*-pyridazin-3-one (**4**) (543.4 mg, 97%).

Reaction of 1 with phenol

Following the *method A*, **5a** and **5b** were obtained in 56 and 16% yields, respectively (purified by column chromatography, with EtOAc : hexane = 1 : 6).

5-Chloro-2-methyl-6-nitro-4-phenoxy-*2H*-pyridazin-3-one (5a)

Pale yellow prisms; mp 105-106 ºC (CH_2Cl_2/hexane); IR (KBr) 3048, 2949, 1685, 1582, 1272 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.83 (s, 3H), 7.02 (m, 2H), 7.22 (m, 1H), 7.39 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 40.6, 116.9, 120.7, 124.9, 129.8, 146.2, 149.8, 155.1, 155.2. Anal. Calcd for $C_{11}H_8N_3O_4Cl$: C, 46.91; H, 2.86; N,14.92. Found: C, 46.83; H, 2.62; N, 15.12.

4-Chloro-2-methyl-6-nitro 5-phenoxy-*2H*-pyridazin-3-one (5b)

Pale yellow prisms; mp 145-147 ºC (CH_2Cl_2/hexane); IR (KBr): 3057, 2949, 1686, 1582, 1272 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.92 (s, 3H), 6.94 (m, 2H), 7.18 (m, 1H), 7.36 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 41.5, 116.2, 124.9, 128.6, 130.1, 146.0, 151.2, 154.9, 158.3. Anal. Calcd for $C_{11}H_8N_3O_4Cl$: C, 46.91; H, 2.86; N, 14.92. Found: C, 47.15; H, 2.58; N, 14.70.

Following the *method B*, compounds (**5a**) and (**5b**) were obtained in 80 and 19% yields, respectively.

Reaction of 1 with p-chlorophenol

Following the *method A*, **6a** and **6b** were obtained in 74 and 15% yields, respectively (purified by column chromatography, with EtOAc : hexane = 1 : 2).

5-Chloro-4-(4-chlorophenoxy)-2-methyl-6-nitro-*2H*-pyridazin-3-one (6a)

Pale yellow prisms; mp 90-91 ºC (CH_2Cl_2/hexane); IR (KBr): 3088, 1667, 1582, 1484, 1359, 1203 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.72 (s, 3H), 6.87 (d, *J* = 9.0 Hz, 2H), 7.24 (d, *J* = 9.0 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 41.2, 118.8, 121.5, 130.4, 130.8, 146.5, 150.0, 154.1, 155.5. Anal. Calcd for $C_{11}H_7N_3O_4Cl_2$: C, 41.80; H, 2.23; N, 13.29. Found: C, 41.50; H, 2.02; N, 13.48.

4-Chloro-5-(4-chlorophenoxy)-2-methyl-6-nitro-*2H*-pyridazin-3-one (6b)

Pale yellow prisms; mp 152 ºC (CH_2Cl_2/hexane); IR (KBr) 2968, 1677, 1590, 1486, 1377 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.85 (s, 3H), 6.82 (d, *J* = 9.0 Hz, 2H), 7.25 (d, *J* = 9.0 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 44.2, 120.2, 120.5, 131.5, 132.9, 148.4, 156.0, 156.1, 160.8. Anal. Calcd for $C_{11}H_7N_3O_4Cl_2$: C, 41.80; H, 2.23; N, 13.29. Found: C, 41.63; H, 2.32; N, 13.41.

Following the *method B*, compounds (**6a**) and (**6b**) were obtained in 72 and 20% yields, respectively.

Reaction of 1 with p-cyanophenol

Following the *method A*, **7a**, **7b**, and **7c** were obtained in 48, 24, and 8% yields, respectively (purified by column chromatography, with EtOAc : hexane = 1 : 2).

5-Chloro-4-(4-cyanophenoxy)-2-methyl-6-nitro-*2H*-pyridazin-3-one (7a)

Colorless prisms; mp 130-131 ºC (CH_2Cl_2/hexane); IR (KBr) 3099, 2999, 2230, 1684, 1497, 1206 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.82 (s, 3H), 7.08 (d, *J* = 6.8 Hz, 2H), 7.68 (d, *J* = 6.8 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 40.8, 108.8, 117.6, 118.0, 122.0, 134.2, 132.5, 148.6, 154.7, 157.8. Anal. Calcd for $C_{12}H_7N_4O_4Cl$: C, 47.00; H, 2.30; N, 18.27. Found: C, 47.23; H, 2.42; N, 18.51.

4-Chloro-5-(4-cyanophenoxy)-2-methyl-6-nitro-*2H*-pyridazin-3-one (7b)

Colorless prisms; mp 189-190 ºC (CH_2Cl_2/hexane); IR (KBr) 3061, 2230, 1676, 1591, 1499, 1286 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.95 (s, 3H), 7.05 (d, *J* = 9.0 Hz, 2H), 7.69 (d, *J* = 9.0 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 42.1, 109.2, 117.1, 118.2, 130.1, 134.9, 143.5, 145.2, 157.9, 158.2. Anal. Calcd for $C_{12}H_7N_4O_4Cl$: C, 47.00; H, 2.30; N, 18.27. Found: C, 47.33; H, 2.12; N, 18.01.

4,5-Bis-(4-cyanophenoxy)-2-methyl-6-nitro-*2H*-pyridazin-3-one (7c)

Colorless prisms; mp 159-160 ºC (CH_2Cl_2/*n*-hexane); IR (KBr) 3098, 2993, 2227, 1677, 1596, 1497, 1214 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.89 (s, 3H), 6.86 (d, *J* = 9.0 Hz, 2H), 7.03 (d, *J* = 9.0 Hz, 2H), 7.58 (d, *J* = 9.0 Hz, 2H), 7.62 (d, *J* = 9.0 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 41.4, 109.1, 109.3, 117.5, 117.7, 118.1, 118.3, 134.5, 134.7, 139.4, 142.0, 144.3, 157.4, 157.7, 158.5. Anal. Calcd for $C_{19}H_{11}N_5O_5$: C, 58.62; H, 2.85; N, 17.99. Found: C, 58.80; H, 3.01; N, 17.72.

Following the *method B*, compounds (**7a**, **7b**, and **7c**) were obtained in 60, 22, and 14% yields, respectively.

Reaction of 1 with p-nitrophenol

Following the *method A*, **8a** and **8b** were obtained in 55 and 17% yields, respectively (purified by column chromatography, with EtOAc : hexane = 1 : 3).

5-Chloro-2-methyl-4-(4-nitrophenoxy)-6-nitro-*2H*-pyridazin-3-one (8a)

Yellow needles; mp 88-89 ºC (CH_2Cl_2/hexane); IR (KBr) 3075, 1674, 1584, 1520, 1347, 1207 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.76 (s, 3H), 7.03 (d, *J* = 9.1 Hz, 2H), 8.19 (d, *J* = 9.1 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 41.2, 117.5, 122.5, 126.3, 126.6,144.9, 148.9, 155.1, 159.5. Anal. Calcd for $C_{11}H_7N_4O_6Cl$: C, 40.45; H, 2.16; N, 17.15. Found: C, 40.23; H, 2.32; N, 17.34.

4-Chloro-2-methyl-5-(4-nitrophenoxy)-6-nitro-*2H*-pyridazin-3-one (8b)

Yellow needles; mp 136-137 ºC (CH_2Cl_2/hexane); IR (KBr) 3072, 1688, 1582, 1517, 1345, 1225 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.98 (s, 3H), 7.10 (d, *J* = 7.1 Hz, 2H), 8.30 (d, *J* = 7.1 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 42.1, 116.6, 126.3, 126.6, 130.2, 144.8, 145.2, 158.2, 159.3. Anal. Calcd for $C_{11}H_7N_4O_6Cl$: C, 40.45; H, 2.16; N, 17.15. Found: C, 40.68; H, 2.22; N, 16.98.

Following the *method B*, compounds (**8a**) and (**8b**) were obtained in 60 and 33% yields, respectively.

Reaction of 1 with 2-mercaptopyrimidine

Following the *method A*, **9a** and **9b** were obtained in 60 and 29% yields, respectively (purified by column chromatography, with EtOAc).

5-Chloro-4-(2-mercaptopyrimidyl)-2-methyl-6-nitro-*2H*-pyridazin-3-one (9a)

Yellow prisms; mp 118-119 ºC (CH_2Cl_2/hexane); IR (KBr) 3034, 2997, 1665, 1556, 1374 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.76 (s, 3H), 7.05 (t like, *J* = 4.8 Hz, 1H), 8.45 (d, *J* = 4.6 Hz, 2H); ^{13}C-NMR (125

MHz, $CDCl_3$) δ 40.2, 117.4, 133.1, 135.8, 144.3, 155.9, 156.8, 166.6. Anal. Calcd for $C_9H_6N_5O_3SCl$: C, 36.07; H, 2.02; N, 23.37; S, 10.70. Found: C, 36.38; H, 2.32; N, 23.59; S, 10.92.

4-Chloro-5-(2-mercaptopyrimidyl)-2-methyl-6-nitro-*2H*-pyridazin-3-one (9b)

Yellow prisms; mp 151-153 ºC (CH_2Cl_2/hexane); IR (KBr) 3040, 1669, 1553, 1378, 1167 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.80 (s, 3H), 7.02 (t like, *J* = 4.8 Hz, 1H), 8.43 (d, *J* = 4.9 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 41.2, 118.2, 133.7, 143.7, 148.0, 157.1, 157.6, 168.0. Anal. Calcd for $C_9H_6N_5O_3SCl$: C, 36.07; H, 2.02; N, 23.37; S, 10.70. Found: C, 36.29; H, 1.98; N, 23.03; S, 10.98.

Following the *method B*, compounds (**9a**) and (**9b**) were obtained in 67 and 25% yields, respectively.

6-Amino-5-chloro-4-(4-methoxyphenoxy)-2-methyl-*2H*-pyridazin-3-one (10)

A mixture of **4** (1.2 g, 3.86 mmol), NH_4Cl (1.2 g, 0.02 mol), Fe (1.0 g, 0.018 mol), $CHCl_3$ (20 mL), and H_2O (20 mL) was refluxed for 2 h. The mixture was cooled to rt, filtered using Celite 545 resin, and washed with $CHCl_3$ (100 mL). The combined filtrate was evaporated under reduced pressure to give a residue, which was purified by column chromatography on silica gel ($CHCl_3$: MeOH = 10 : 1) to give **10** (1.03 g, 95%) as colorless prisms, mp 178-179 °C (CH_2Cl_2/hexane); IR (KBr) 3350, 3280, 2950, 1630, 1590 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.60 (s, 3H), 3.77 (s, 3H), 4.45 (s, 2H), 6.83 (d, *J* = 10.5 Hz, 2H), 6.92 (d, *J* = 10.5 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 39.14, 55.65, 114.62, 117.67, 119.80, 144.67, 148.92, 149.78, 154.54, 156.02. Anal. Calcd for $C_{12}H_{12}N_3O_3Cl$: C, 51.16; H, 4.29; N, 14.92. Found: C, 51.38; H, 4.40; N, 14.78.

6-Amino-4-(4-methoxyphenoxy)-2-methyl-*2H*-pyridazin-3-one (11)

A mixture of **10** (500 mg, 1.77 mmol), Pd/C (250 mg), and MeOH (30 mL) was stirred for 5 h under hydrogen atmosphere at rt. The mixture was filtered using Celite 545 resin and washed with $CHCl_3$ (50 mL). The combined filtrate was evaporated under reduced pressure to give a residue, which was purified by column chromatography on silica gel (EtOAc : hexane = 1 : 1) to give **11** (350 mg, 80%) as yellow prisms, mp 200-202 °C (CH_2Cl_2/hexane); IR (KBr) 3480, 3080, 2950, 1740, 1680, 1590 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.64 (s, 3H), 3.82 (s, 3H), 3.97 (s, 2H), 5.83 (s, 1H), 6.92 (d, *J* = 9.0 Hz, 2H), 7.02 (d, *J* = 9.0 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 39.29, 55.65, 102.01, 122.05, 146.68, 147.24, 154.81, 156.78, 157.55. Anal. Calcd for $C_{12}H_{13}N_3O_3$: C, 58.29; H, 5.30; N, 17.00. Found: C, 58.40; H, 5.40; N, 17.22.

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