

Hyun-A Chung, Young-Jin Kang, D. H. Kweon, Woo Song Lee[‡]
and Yong-Jin Yoon*

Department of Chemistry, Gyeongsang National University, Chinju 660-701, Korea
Received March 8, 2000

This paper presents the synthesis of 1-[(pyrazol-3-yl)methyl]pyridazin-6-ones from ethyl 4-(4,5-dichloro-6-oxopyridazin-1-yl)-3-oxobutanoate.

J. Heterocyclic Chem., **37**, 1443 (2000).

In connection with our research program for the synthesis of novel pyridazinone derivatives, we required some 1-[(pyrazol-3-yl)methyl]pyridazin-6-ones containing one active methylene. The most widely known synthetic route to pyrazoles is the reaction of 1,3-dicarbonyl compounds and hydrazines [1,2]. Therefore, alkyl 4-(6-oxopyridazin-1-yl)-3-oxobutanoates are useful material for the synthesis of 1-[(pyrazol-3-yl)methyl]pyridazin-6-ones. In accordance with literature [1], ethyl 3-oxobutanoate is also reacted with phenyl hydrazine to give 1-phenyl-3-methylpyrazol-5-one. Therefore, we attempted to prepare 1-[(pyrazol-3-yl)methyl]pyridazin-6-ones from ethyl 4-(4,5-dichloro-6-oxopyridazin-1-yl)-3-oxobutanoate.

In this paper, we report the synthesis of some 4,5-dichloro-1-[(pyrazol-3-yl)methyl]pyridazin-6-one derivatives. In a previous report [3], we synthesized methyl 4-(4,5-dichloro-6-oxopyridazin-1-yl)-3-oxobutanoate from methyl 4-bromoacetoacetate in the presence of potassium cyanide in *N,N*-dimethylformamide in low yield. Because of the low yield, we attempted to develop a novel synthetic method to prepare **2**.

Since pyridazinones are a good source of an ambident anion under basic conditions, the alkylation of pyridazin-6-ones under basic conditions give the corresponding *N*-alkyl and *O*-alkyl products. According to S. K. Kim, *et al.* [4], the reaction of 4,5-dichloropyridazin-6-one with alkyl halides using tetrabutylammonium bromide/potassium hydroxide/benzene system gave regioselectively the corresponding *N*-alkyl derivatives. Therefore, we also attempted to synthesize **2** using Kim's system [4].

Reaction of **1** with ethyl 4-chloro-3-oxobutanoate, potassium hydroxide, tetrabutylammonium bromide in benzene under reflux gave **2** in good yield. The structure of **2** was established by ir, nmr and elemental analysis. The infrared spectrum revealed the absorption bands of three carbonyl groups at 1755, 1726 and 1664 cm^{-1} . The proton magnetic resonance spectrum showed the proton signals for two methylenes, one ethyl group and one aromatic proton. The ^{13}C nmr spectrum also showed the signals for the carbons of three carbonyl groups and one ethyl group involving the ring carbons of pyridazinone.

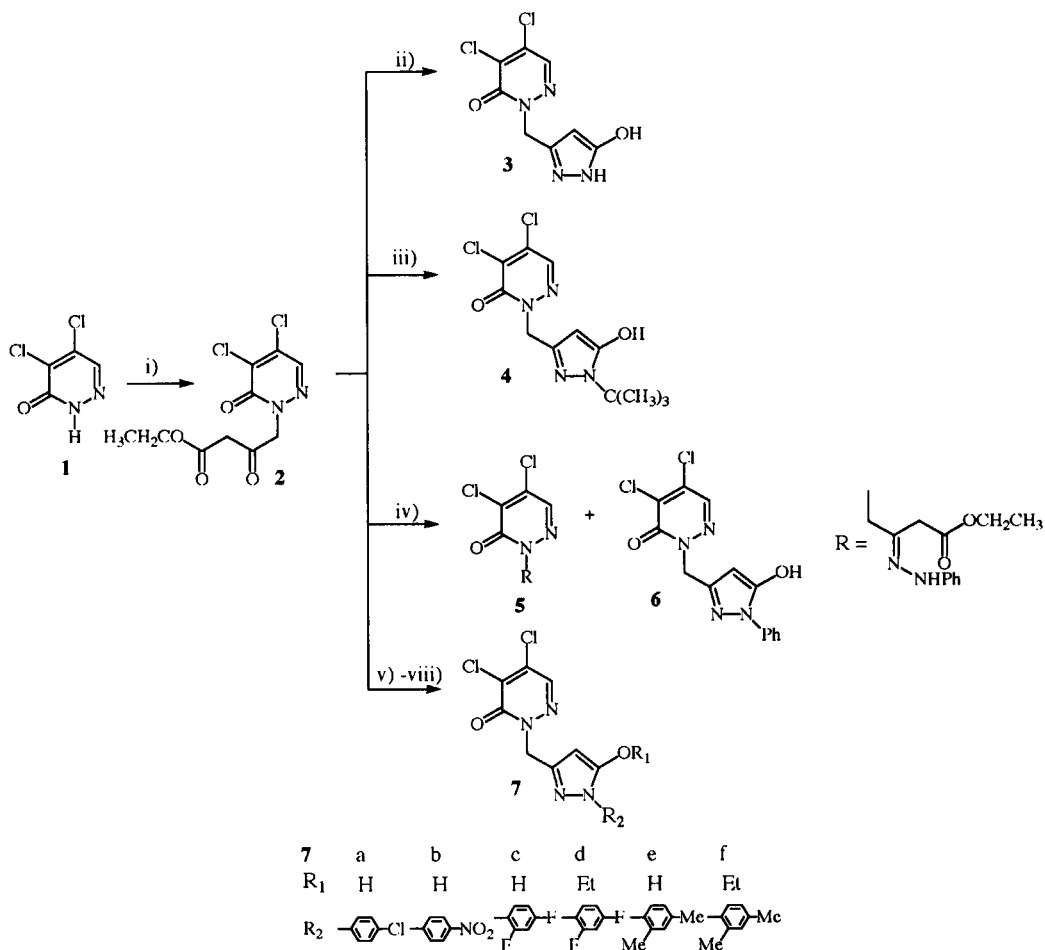
On the other hand, treatment of **2** with hydrazine monohydrate in boiling ethanol afforded the corresponding 4,5-dichloro-1-[(5-hydroxypyrazol-3-yl)methyl]-

pyridazin-6-one (**3**) in low yield. Reaction of **2** with *tert*-butylhydrazine in boiling ethanol gave **4** in 74% yield. Compound **2** was reacted with phenylhydrazine in boiling ethanol to yield hydrazone **5** and the corresponding pyrazole **6**. According to our observation by monitoring tlc, compound **5** was formed in the initial step and then cyclized to **6** in the final step. Cyclization of **2** with *p*-chlorophenylhydrazine or *p*-nitrophenylhydrazine in boiling ethanol yielded pyrazole **7a** or **7b** in good yield, respectively. Whereas, reaction of **2** with 2,4-difluorophenylhydrazine in ethanol afforded the corresponding 5-hydroxypyrazole **7c** (63%) and 5-ethoxypyrazole **7d** (18%). Treatment of **2** with 2,4-dimethylphenylhydrazine in ethanol also gave 5-hydroxypyrazole **7e** (56%) and 5-ethoxypyrazole **7f** (30%).

The structures of **3-7** were established by ir, nmr and elemental analyses. In the infrared spectra of **3, 4, 6** and **7**, absorption bands were observed the amide carbonyl, the NH for **3** and hydroxyl groups for all except **7d** and **7f**. The infrared spectrum of **5**, however, absorption bands corresponding to both carbonyls groups and the NH are observed. The proton magnetic resonance spectra of **3, 4, 6** and **7a-f** showed proton signals corresponding to the CH_2 in the α -position at δ 5.05 - 5.22, the CH in the 4-position of pyrazole at δ 5.28 - 5.80, and the CH in the 3-position of pyridazinone at δ 8.20 - 8.24. In the ^1H nmr for **3, 4, 6, 7** except for **7c, 7d** and **7f**, the proton signal corresponding to the OH is observed at δ 8.63 - 12.42 range that corresponds to the protons of phenyl groups for **6** and **7**. The ^1H nmr spectrum for **3** and **4** revealed proton signals for the NH group of **3** or *tert*-butyl group for **4**. The proton magnetic resonance spectrum of **5** revealed proton signals for two CH_2 , one CH and one NH corresponding to protons of the phenyl and ethyl groups. In the proton resonance spectra of **7d** and **7f**, proton signals corresponding to the ethyl group rather than the hydroxyl group were detected. The ^{13}C nmr spectra of **3 - 7** showed signals of one carbonyl group except for **5**. The ^{13}C nmr of **5** showed the signals of two carbonyls at δ 158.8 and δ 170.9 ppm, whereas the signal of carbonyl group at C-3 of butanoate was not observed.

Finally, the carbonyls on the side chain at the N-1 position are more reactive with hydrazines than the carbons at C-4 and C-5 on the ring of pyridazin-6-one under our conditions. Therefore, ethyl 4-(6-oxopyridazin-1-yl)-3-oxobutanoate is useful material for the synthesis of

Scheme 1



i) $\text{ClCH}_2\text{COCH}_2\text{COOEt}$, KOH, tetrabutylammonium bromide, benzene.

ii) $\text{NH}_2\text{NH}_2 \cdot \text{H}_2\text{O}$, ethanol, reflux. iii) $\text{NH}_2\text{NHC}(\text{CH}_3)_3$, ethanol, reflux.

iv) Phenylhydrazine, ethanol, reflux. v) *p*-chlorophenylhydrazine $\cdot\text{HCl}$, ethanol, reflux.

vi) 4-nitrophenylhydrazine, ethanol, reflux. vii) 2,4-difluorophenylhydrazine $\cdot\text{HCl}$, ethanol, reflux.

viii) 2,4-dimethylphenylhydrazine $\cdot\text{HCl}$, ethanol, reflux.

the corresponding 1-[(pyrazol-3-yl)methyl]pyridazin-6-one derivatives.

Further work including the chemical transformation and a biological activity of novel derivatives is under way in our laboratory.

EXPERIMENTAL

Melting points were determined with a Thomas-Hoover capillary apparatus and are uncorrected. Magnetic resonance spectra were obtained on a Varian Unity Plus 300 or a Bruker FTNMR-DRX 500 spectrometer with chemical shift values reported in δ units (part per million) relative to an internal standard (tetramethylsilane). Infrared spectral data were obtained on a Hitachi 270-50 spectrophotometer. Elemental analyses were

performed with a Perkin Elmer 240C. Open-bed chromatography was carried out on silica gel 60 (70-230 mesh, Merck) using gravity flow. The column was packed as slurries with the elution solvent.

Ethyl 4-(4,5-dichloro-6-oxopyridazin-1-yl)-3-oxobutanoate (2).

A mixture of **1** (10 g, 60.6 mmol), ethyl 4-chloro-3-oxobutanoate (12.3 ml, 90 mmol), potassium hydroxide (5.1 g, 90 mmol), tetrabutylammonium bromide (6 g, 18.6 mmol) and benzene (150 ml) was stirred for 7 hours at 60–70°. After cooling to room temperature, the mixture was filtered and washed with acetone (10 ml \times 10). The combined filtrate was evaporated under reduced pressure. The residue was applied to the top of an open-bed silica gel column (3 \times 8 cm). The column was eluted with chloroform/*n*-hexane (1:1, v/v). Fractions containing the product ($R_f = 0.2$, chloroform) were combined and

evaporated under reduced pressure. The resulting residue was recrystallized from diethyl ether/*n*-hexane (1:0.5, v/v) to give **2** as white crystals in 81% (14.38 g) yield. mp 139-140°; ir (potassium bromide): 3102, 3073, 2996, 2974, 2842, 1755, 1726, 1664, 1583, 1416, 1368, 1327, 1278, 1110, 1032, 894, 742 cm⁻¹; ¹H nmr (deuteriochloroform): δ 1.23 (t, 3H, J = 7.1), 3.53 (s, 2H), 4.16 (q, 2H, J = 7.1, 7.1, 7.2), 5.07 (s, 2H), 7.74 ppm (s, 1H₃); ¹³C nmr (deuteriochloroform): δ 14.4, 47.7, 61.3, 62.3, 134.8, 136.7, 137.5, 156.9, 166.6, 194.6 ppm.

Anal. Calcd. For C₁₀H₁₀N₂O₄Cl₂: C, 40.98; H, 3.44; N, 9.56. Found: C, 41.02; H, 3.56; N, 9.61.

4,5-Dichloro-2-[(5-hydroxypyrazol-3-yl)methyl]pyridazin-3-one (**3**).

A mixture of **2** (0.5 g, 1.71 mmoles), hydrazine monohydrate (0.51 g, 10.19 mmoles) and ethanol (20 ml) was refluxed for 0.5 hours. After evaporating the solvent under reduced pressure, the product was extracted with methanol (20 ml x 3). The solution was dried over anhydrous magnesium sulfate and coevaporated with silica gel (2 g) under reduced pressure. The resulting gel was applied to the top of an open-bed silica gel column (3 x 10 cm). The column was eluted with chloroform/methanol (9:1, v/v). Fractions containing the product were combined and evaporated under reduced pressure. The crude product was recrystallized from methanol/chloroform (1:10, v/v) to give **3** in 37% (0.166 g) yield. mp 202-204°; ir (potassium bromide): 3400-2500 (m), 1670, 1636, 1545, 1450, 1340, 1218, 1125, 1020, 800 cm⁻¹; ¹H nmr (dimethyl sulfoxide-d₆): δ 5.15 (s, 2H_α), 5.74 (s, 1H₄), 8.20 (s, 1H₆), 8.63 ppm (s, OH, deuterium oxide exchangeable); ¹³C nmr (dimethyl sulfoxide-d₆): δ 46.6, 64.3, 87.7, 104.1, 126.8, 141.6, 154.9, 155.8 ppm.

Anal. Calcd. For C₈H₆N₄O₂Cl₂: C, 36.81; H, 2.32; N, 21.46. Found: C, 36.96; H, 2.43; N, 21.75.

2-[(1-*tert*-butyl-5-hydroxypyrazol-3-yl)methyl]-4,5-dichloropyridazin-3-one (**4**).

A solution of **2** (0.5 g, 1.71 mmoles), *tert*-butylhydrazine hydrochloride (0.3 g, 2.56 mmoles) and ethanol (20 ml) was refluxed for 20 hours. After cooling to room temperature, the mixture was coevaporated with silica gel (1.5 g) under reduced pressure. The resulting gel was applied to the top of an open-bed silica gel column (2 x 15 cm). The column was eluted with chloroform/diethyl ether (9.5:0.5, v/v). Fractions containing **4** (R_f = 0.55, chloroform/methanol = 9:1, v/v) were combined and evaporated under reduced pressure. The residue was recrystallized from diethyl ether to afford **4** in 74% (0.4 g) yield. mp 188-189°; ir (potassium bromide): 3200-2500 (m), 1680, 1570, 1410, 1320, 1225, 1130, 970 cm⁻¹; ¹H nmr (dimethyl sulfoxide-d₆): δ 1.48 (s, 9H), 5.05 (s, 2H_α), 5.28 (s, 1H₄), 8.20 (s, 1H₆), 10.69 ppm (s, OH, deuterium oxide exchangeable); ¹³C nmr (dimethyl sulfoxide-d₆): δ 27.8, 50.1, 56.7, 86.1, 132.2, 135.0, 135.3, 141.5, 152.3, 154.9 ppm.

Anal. Calcd. For C₁₂H₁₄N₄O₂Cl₂: C, 45.44; H, 4.45; N, 17.66. Found: C, 45.76; H, 4.68; N, 17.93.

Ethyl 4-(4,5-Dichloro-6-oxopyridazin-1-yl)-3-phenylhydrazinobutanoate (**5**) and 4,5-Dichloro-2-[(5-hydroxy-1-phenylpyrazol-3-yl)methyl]pyridazin-3-one (**6**).

A mixture of **2** (1 g, 3.41 mmoles), phenylhydrazine (0.6 g, 5.12 mmoles) and ethanol (30 ml) was refluxed for 40 minutes. After cooling to room temperature, the mixture was coevaporated with silica gel (2 g) under reduced pressure. The residue was

applied to the top of an open-bed silica gel column (2 x 25 cm). The column was eluted with methylene chloride. Fractions containing **5** (R_f = 0.7, chloroform/diethyl ether = 9:1, v/v) were combined and evaporated under reduced pressure. The resulting residue was recrystallized from methylene chloride/*n*-hexane (1:2, v/v) to afford **5** as yellow crystals in 41% (0.54 g) yield. mp 114-116°; ir (potassium bromide): 3350, 3060, 3000, 2910, 1760, 1740, 1650, 1605, 1500, 1400, 1380, 1350, 1320, 1260, 1220, 1190, 1130, 970, 880, 750 cm⁻¹; ¹H nmr (dimethyl sulfoxide-d₆): δ 1.73 (t, 3H, J = 7.1), 3.57 (s, 2H), 4.06 (q, 2H, J = 7.1, 7.1, 7.1), 4.93 (s, 2H), 6.73 - 7.17 (m, aromatic 5H), 8.23 (s, 1H₃), 9.38 ppm (bs, NH, deuterium oxide exchangeable); ¹³C nmr (dimethyl sulfoxide-d₆): δ 16.8, 36.0, 59.9, 63.5, 115.2, 121.9, 131.7, 135.7, 136.5, 138.6, 138.8, 148.3, 158.8, 170.9 ppm.

Anal. Calcd. For C₁₆H₁₆N₄O₃Cl₂: C, 50.15; H, 4.21; N, 14.62. Found: C, 50.36; H, 4.35; N, 14.80.

Fractions containing **6** (R_f = 0.1, chloroform/diethyl ether = 9:1, v/v) were combined and evaporated under reduced pressure. The residue was recrystallized from diethyl ether to give **6** in 25% (0.3 g) yield. mp 190-191°; ir (potassium bromide): 3100-2400 (m), 1660, 1600, 1560, 1400, 1300, 1218, 1140, 1020, 960, 880, 750 cm⁻¹; ¹H nmr (dimethyl sulfoxide-d₆): δ 5.18 (s, 2H_α), 5.51 (s, 1H₄), 7.24-7.69 (m, aromatic, 5H), 8.22 (s, 1H₆), 11.67 ppm (s, OH, deuterium oxide exchangeable); ¹³C nmr (dimethyl sulfoxide-d₆): δ 48.6, 85.1, 119.1, 123.7, 126.9, 131.0, 134.0, 134.2, 136.6, 144.6, 151.4, 153.7 ppm.

Anal. Calcd. For C₁₄H₁₀N₄O₂Cl₂: C, 49.87; H, 2.99; N, 16.62. Found: C, 49.98; H, 3.02; N, 16.81.

4,5-Dichloro-2-[[1-(4-chlorophenyl)-5-hydroxypyrazol-3-yl]methyl]pyridazin-3-one (**7a**).

A mixture of **2** (1 g, 3.41 mmoles), *p*-chlorophenylhydrazine hydrochloride (0.9 g, 5.12 mmoles) and ethanol (30 ml) was refluxed for 20 minutes. After evaporating the solvent under reduced pressure, the residue was applied to the top of an open-bed silica gel column (2 x 20 cm). The column was eluted with methylene chloride. Fractions containing the product were combined and evaporated under reduced pressure. The residue was triturated in diethyl ether. The mixture was filtered and dried in air to give **7a** in 83% (1.1 g) yield. mp 216-217°; ir (potassium bromide): 3200-2400 (m), 1665, 1570, 1505, 1420, 1360, 1310, 1230, 1160, 1110, 980, 840 cm⁻¹; ¹H nmr (dimethyl sulfoxide-d₆): δ 5.18 (s, 2H_α), 5.53 (s, 1H₄), 7.49 (d, aromatic 2H, J = 8.8), 7.74 (d, aromatic 2H, J = 8.8), 8.21 (s, 1H₆), 11.90 ppm (s, OH, deuterium oxide exchangeable); ¹³C nmr (dimethyl sulfoxide-d₆): δ 52.0, 88.8, 123.8, 130.4, 131.2, 134.5, 137.5, 137.7, 138.9, 148.5, 155.1, 157.1 ppm.

Anal. Calcd. For C₁₄H₉N₄O₂Cl₃: C, 45.25; H, 2.44; N, 15.08. Found: C, 45.30; H, 2.64; N, 15.23.

4,5-Dichloro-2-[[1-(4-nitrophenyl)-5-hydroxypyrazol-3-yl]methyl]pyridazin-3-one (**7b**).

A mixture of **2** (0.5 g, 1.71 mmoles), *p*-nitrophenylhydrazine (0.4 g, 2.56 mmoles) and ethanol (20 ml) was refluxed for 62 hours. After cooling to room temperature, the mixture was filtered. The filtrate was coevaporated with silica gel (3 g) under reduced pressure. The resulting gel was applied to the top of an open-bed silica gel column (3 x 12 cm). The column was eluted with chloroform. Fractions containing the product (R_f = 0.1, chloroform/diethyl ether = 9:1, v/v) were combined and evaporated under reduced pressure. The residue was recrystallized from chloroform/diethyl ether

(1:3, v/v) to give **7b** in 77% (0.5 g) yield. mp 184-185°; ir (potassium bromide): 3300-2800 (m), 1750, 1680, 1640, 1610, 1590, 1530, 1340, 1230, 1125, 980, 865, 760 cm⁻¹; ¹H nmr (dimethyl sulfoxide-d₆): δ 5.21 (s, 2H_α), 5.57 (s, 1H₄), 8.04-8.07 (m, aromatic 2H), 8.23 (s, 1H₆), 8.26-8.33 (m, aromatic 2H), 12.42 ppm (bs, OH, deuterium oxide exchangeable); ¹³C nmr (dimethyl sulfoxide-d₆): δ 51.8, 89.4, 121.5, 126.3, 137.6, 134.4, 137.5, 145.1, 145.4, 150.2, 156.1, 157.1 ppm.

Anal. Calcd. For C₁₄H₉N₅O₄Cl₂: C, 44.00; H, 2.37; N, 18.33. Found: C, 44.11; H, 2.49; N, 18.48.

4,5-Dichloro-2-[[1-(2,4-difluorophenyl)-5-hydroxypyrazol-3-yl]methyl]pyridazin-3-one (**7c**) and 4,5-Dichloro-2-[[1-(2,4-difluorophenyl)-5-ethoxypyrazol-3-yl]methyl]pyridazin-3-one (**7d**).

A mixture of **2** (1 g, 3.41 mmoles), 2,4-difluorophenylhydrazine hydrochloride (0.9 g, 5.12 mmoles) and ethanol (30 ml) was refluxed for 30 minutes. After evaporating the solvent under reduced pressure, the residue was applied to the top of an open-bed silica gel column (2 x 18 cm). The column was eluted with chloroform. Fractions containing **7d** (R_f = 0.8, chloroform/diethyl ether = 9:1, v/v) were combined and evaporated under reduced pressure. The residue was recrystallized from diethyl ether/*n*-hexane (1:3, v/v) to give **7d** in 18% (0.25 g) yield. mp 110-112°; ir (potassium bromide): 3150, 3090, 3050, 3000, 1675, 1610, 1565, 1535, 1418, 1270, 1220, 1150, 1110, 1045, 960, 850 cm⁻¹; ¹H nmr (dimethyl sulfoxide-d₆): δ 1.24 (t, 3H), J = 7.1), 4.13 (q, 2H, J = 6.9, 7.0, 7.1), 5.22 (s, 2H_α), 5.80 (s, 1H₄), 7.21-7.56 (m, aromatic 3H), 8.24 ppm (s, 1H₆); ¹³C nmr (dimethyl sulfoxide-d₆): δ 16.5, 52.6, 70.3, 87.2, 107.3, 114.4, 124.2, 132.2, 135.5, 138.3, 150.0, 157.5, 157.9, 159.5, 159.6, 162.9 ppm.

Anal. Calcd. For C₁₆H₁₂N₄O₂Cl₂F₂: C, 47.90; H, 3.01; N, 13.96. Found: C, 48.01; H, 3.24; N, 14.08.

Fractions containing **7c** (R_f = 0.18, chloroform/diethyl ether = 9:1, v/v) were combined and evaporated under reduced pressure. The residue was triturated in diethyl ether. The mixture was filtered and dried in air to give **7c** in 63% (0.8 g) yield. mp 215-216°; ir (potassium bromide): 3200-2400 (m), 1660, 1570, 1540, 1408, 1360, 1330, 1220, 1145, 1100, 960, 845 cm⁻¹; ¹H nmr (dimethyl sulfoxide-d₆): δ 5.17 (s, 2H_α), 5.47 (s, 1H₄), 7.18-7.52 (m, aromatic 3H), OH no detection; ¹³C nmr (dimethyl sulfoxide-d₆): δ 51.6, 86.8, 106.0, 112.9, 123.4, 131.1, 134.1, 137.1, 148.6, 155.1, 156.7, 158.5, 161.7, 163.6 ppm.

Anal. Calcd. For C₁₄H₈N₄O₂Cl₂ F₂: C, 45.06; H, 2.16; N, 15.01. Found: C, 45.24; H, 2.30; N, 15.22.

4,5-Dichloro-2-[[1-(2,4-dimethylphenyl)-5-hydroxypyrazol-3-yl]methyl]pyridazin-3-one (**7e**) and 4,5-Dichloro-2-[[1-(2,4-dimethylphenyl)-5-ethoxypyrazol-3-yl]methyl]pyridazin-3-one (**7f**).

A mixture of **2** (1 g, 3.41 mmoles), 2,4-dimethylphenylhydrazine hydrochloride (0.88 g, 5.12 mmoles) and ethanol (20 ml) was refluxed for 2.5 hours. After cooling to room

temperature, the mixture was coevaporated with silica gel (4 g) under reduced pressure. The resulting gel was applied to the top of an open-bed silica gel column (3 x 15 cm). The column was eluted with chloroform. Fractions containing **7f** (R_f = 0.75, chloroform/methanol = 9:1, v/v) were combined and evaporated under reduced pressure. The residue was recrystallized from diethyl ether/*n*-hexane (1:3, v/v) to give **7f** as yellowish crystals in 30% (0.4 g) yield. mp 115-116°; ir (potassium bromide): 3150, 3100, 3060, 2950, 1675, 1560, 1530, 1420, 1400, 1230, 1160, 1130, 1040, 970, 890 cm⁻¹; ¹H nmr (dimethyl sulfoxide-d₆): δ 1.21 (t, 3H, J = 7.1), 1.98 (s, 3H), 2.31 (s, 3H), 4.07 (q, 2H, J = 7.1, 7.0, 7.1), 5.22 (s, 2H_α), 5.74 (s, 1H₄), 7.08-7.13 (m, aromatic 3H), 8.22 ppm (s, 1H₆); ¹³C nmr (dimethyl sulfoxide-d₆): δ 14.3, 17.0, 20.5, 50.6, 67.5, 84.2, 126.8, 127.2, 131.1, 133.0, 134.1, 134.6, 135.9, 136.1, 138.1, 146.1, 154.9, 155.6 ppm.

Anal. Calcd. For C₁₈H₁₈N₄O₂Cl₂: C, 54.97; H, 4.61; N, 14.25. Found: C, 55.01; H, 4.69; N, 14.42.

Fractions containing **7e** (R_f = 0.8, chloroform/methanol = 9:1, v/v) were also combined and evaporated under reduced pressure. The residue was triturated in chloroform and filtered to give **7e** as brownish crystals in 56% (0.7 g) yield. mp 180-181°; ir (potassium bromide): 3200-2400 (m), 1670, 1556, 1420, 1340, 1225, 1130, 970 cm⁻¹; ¹H nmr (dimethyl sulfoxide-d₆): δ 2.00 (s, 3H), 2.31 (s, 3H), 5.16 (s, 2H_α), 5.44 (s, 1H₄), 7.07-7.12 (m, aromatic 3H), 8.20 (s, 1H₆), 11.13 ppm (bs, OH, deuterium oxide exchangeable); ¹³C nmr (dimethyl sulfoxide-d₆): δ 18.6, 21.9, 52.1, 86.5, 128.0, 128.6, 132.4, 134.3, 135.9, 136.1, 137.2, 137.5, 139.1, 147.2, 154.8, 157.0 ppm.

Anal. Calcd. For C₁₆H₁₄N₄O₂Cl₂: C, 52.62; H, 3.86; N, 15.34. Found: C, 52.78; H, 3.97; N, 15.56.

Acknowledgments.

This work was supported by the Brain Korea 21 Project.

REFERENCES AND NOTES

- [1] BK21-School of Molecular Science, Dept. of Chemistry, Korea Advanced Institute of Science and Technology, Taejon 305-701, Korea.
- [2] J. A. Joule, K. Mills and G. F. Smith, *Heterocyclic Chemistry*, 3rd Ed, Chapman and Hall, 2-6 Boundary Row, London SE1 8HN, UK, 1996, p402.
- [3] A. R. Katritzky, FRS, *Comprehensive Heterocyclic Chem.*, vol. 5, Pergamon Press, Ltd., Oxford, 1984, p280.
- [4] S. Y. Choi, S. C. Shin and Y. J. Yoon, *Bull. Kor. Chem. Soc.*, 11(3), 228 (1990).
- [5] S. K. Kim, S. D. Cho, D. H. Kweon, Y. J. Yoon, J. H. Kim and J. N. Heo, *J. Heterocyclic Chem.*, 34, 209 (1997).