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Syntheses of 3- and 4-Alkylaminomethylpyridazines[1]

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Several 3- and 4-alkylaminomethylpyridazines were prepared from 3-hydroxypyridazine 1-oxide and 3-hydroxy-6-chloropyridazine 1-oxide, respectively, using the Mannich reaction.

3,5-Bis(morpholinomethyl)pyridazine was analogously prepared from 3-hydroxypyridazine 1-oxide.

Pyridazine derivatives have recently received much attention from their unique reactions, and also, since many pyridazine derivatives were found to possess plant growth inhibitory and potential therapeutic effects, many syntheses for pyridazines have been developed.

As shown in Chart 1, 3-hydroxypyridazine (I) exists as the alternative lactam form (I'), while 3-hydroxypyridazine 1-oxide (II) predominantly exists as the hydroxy form II. This fact suggests that II is a potential phenol, though the hydroxyl function is adjacent to the ring nitrogen.[3,4]

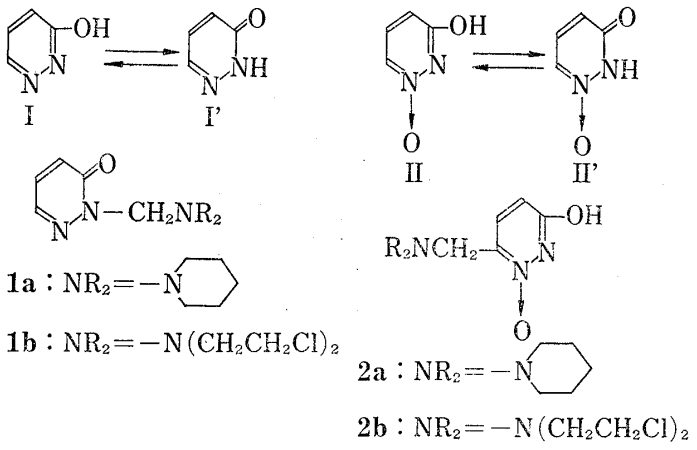

Chart 1

As a matter of fact, we have reported that the Mannich reaction of I using formalin and such a secondary amine as piperidine or 2,2'-dichlorodiethylamine gives the corresponding N-Mannich bases,[5] **1a** and **1b**, while, in contrast, the same reaction of II does the C-Mannich bases,[4,6] 3-hydroxy-6-piperidinomethyl- (**2a**) and 3-hydroxy-6-(2,2'-dichlorodiethylaminomethyl)-pyridazine 1-oxide (**2b**), both in good yields.

This paper describes the preparation of 3- and 4-alkylaminomethylpyridazines as an application of the Mannich reaction of this type.

When II was treated with an equimolar mixture of 37% formalin and such a secondary amine as dimethylamine, dibenzylamine, pyrrolidine, morpholine or 4-methylpiperidine, in ethanol at room temperature, 3-hydroxy-6-alkylaminomethylpyridazine 1-oxides were pro-

1) This work was presented at the 5th Symposium of Heterocyclic Chemistry (November 15, 1972, Gifu). The preceding paper: S. Kamiya, G. Okusa and H. Hirakawa, *Chem. Pharm. Bull.* (Tokyo), **18**, 632 (1970).
2) Location: *a) Kamiyoga 1-18-1, Setagaya, Tokyo; b) Funakoshi 1-45, Yokosuka.*
3) H. Igeta, *Chem. Pharm. Bull.* (Tokyo), **7**, 938 (1959).
4) S. Kamiya, G. Okusa, M. Osada, M. Kumagai, A. Nakamura and K. Koshinuma, *Chem. Pharm. Bull.* (Tokyo), **16**, 5 (1968).
5) S. Kamiya, A. Nakamura, T. Itai, K. Koshinuma and G. Okusa, *Yakugaku Zasshi*, **86**, 1099 (1966).
6) *a)* G. Okusa, S. Kamiya and T. Itai, *Chem. Pharm. Bull.* (Tokyo), **15**, 1172 (1967); *b)* G. Okusa, M. Osada and S. Kamiya, *ibid.*, **15**, 1733 (1967).

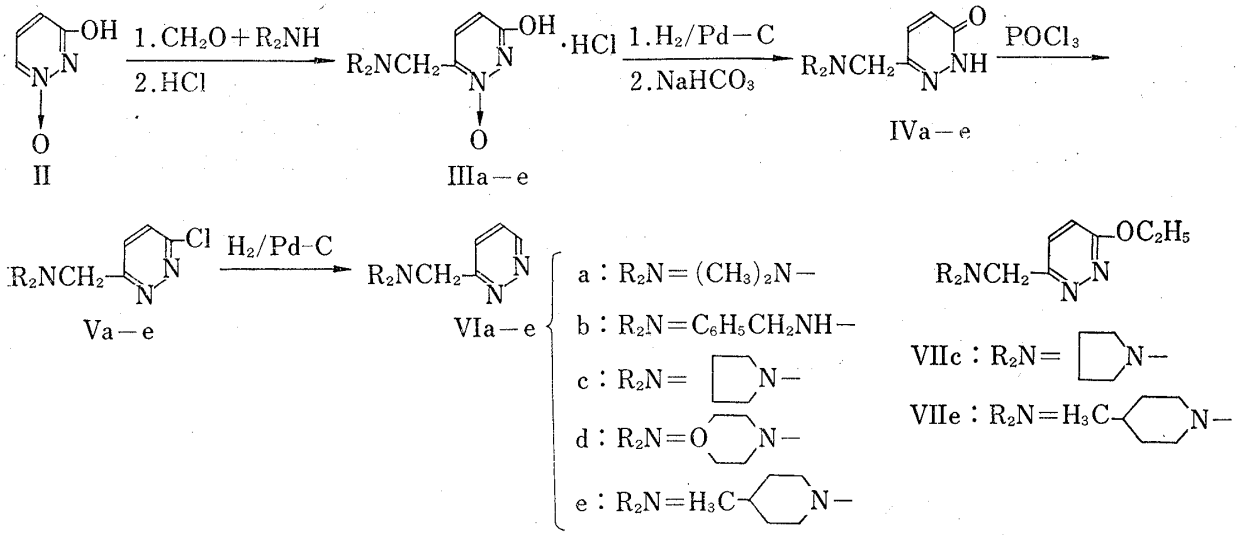

Chart 2

duced as 1: 1 salts with II in 70—90% yields. These salts were converted into hydrochlorides IIIa—e by treatment with hydrochloric acid, simultaneously recovering the starting material II.

Catalytic deoxidation of IIIa—e in the presence of palladium-on-charcoal followed by neutralization with sodium bicarbonate, gave 6-alkylaminomethyl-3(2H)-pyridazinones (IVa—e) in nearly quantitative yields. In the case of IIIb the product was 6-benzylaminomethyl-3(2H)-pyridazinone (IVb). Compounds IVa—e were subsequently treated with phosphorus oxychloride, and the resulting 3-chloro derivatives Va—e were catalytically dehalogenated to give 6-alkylaminomethylpyridazines (VIa—e), *i.e.* 3-alkylaminomethylpyridazines. Overall yields of these 3-alkylaminomethylpyridazines from II reached 25—35%.

The reaction of Vc and Ve with sodium ethoxide gave 3-ethoxy-6-pyrrolidinomethyl- (VIIc) and 3-ethoxy-6-(4-methylpiperidinomethyl)-pyridazine (VIIe), respectively.

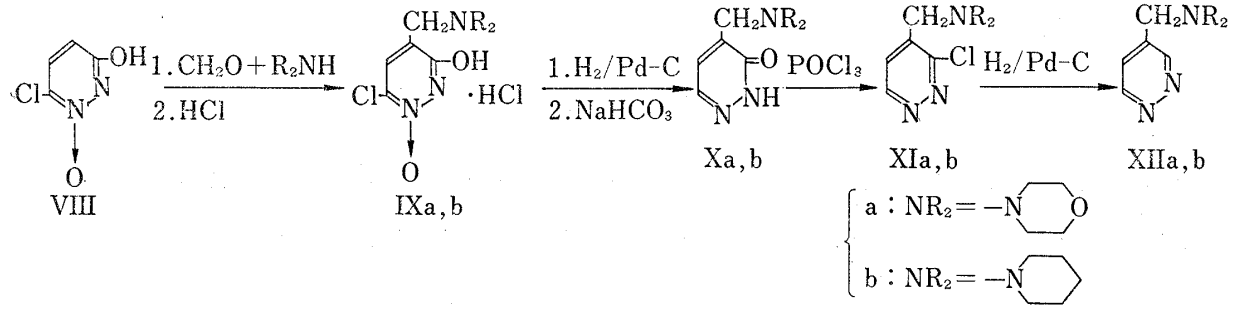

Chart 3

Then, as shown in Chart 3, the synthesis of 4-alkylaminomethylpyridazines (XII) was successfully done by the Mannich reaction of 3-hydroxy-6-chloropyridazine 1-oxide (VIII) which is also a potential phenol due to the presence of the 1-oxide group.[4]

When VIII was allowed to react with an equimolar mixture of 37% formalin and a secondary amine such as morpholine or piperidine at room temperature, 3-hydroxy-4-morpholinomethyl- and 3-hydroxy-4-piperidinomethyl-6-chloropyridazine 1-oxide were produced as salts with VIII in 70—80% yields. These salts were converted into the corresponding hydrochlorides, IXa and IXb, by treatment with hydrochloric acid. Catalytic deoxidation of IXa and IXb with palladium-on-charcoal followed by neutralization with sodium bicarbonate, gave 4-morpholinomethyl- (Xa) and 4-piperidinomethyl-3(2H)-pyridazinone (Xb) in both nearly quantitative yields.

Subsequently, Xa and Xb were treated with phosphorus oxychloride, and the resulting 3-chloro derivatives, XIa and XIb, were catalytically dehalogenated to give 4-morpholinomethyl- (XIIa) and 4-piperidinomethyl-pyridazine (XIIb), respectively. Overall yields of these 4-alkylaminomethylpyridazines calculated from VIII were both about 30%.

Catalytic reduction of XIIb over palladium-on-charcoal afforded 4-methylpyridazine.

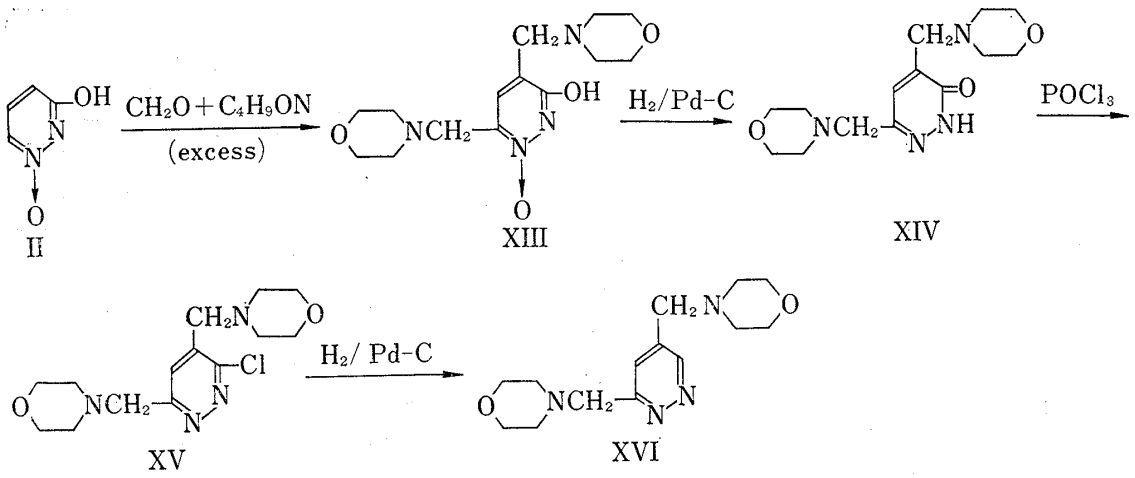

Chart 4

In the same manner as illustrated in Chart 4, 3,5-bis(morpholinomethyl)pyridazine (XVI) was prepared from II in an overall yield of 45%. Namely, treatment of II with excess amounts of 37% formalin and morpholine gave 4,6-bis-C-Mannich base XIII.[6a] Catalytic deoxidation of XIII followed by chlorination and dehalogenation, gave 4,6-bis(morpholinomethyl)-pyridazine (XVI), *i.e.* 3,5-bis(morpholinomethyl)pyridazine.

The nuclear magnetic resonance (NMR) parameters of these 3- and 4-alkylaminomethylpyridazines were all reasonable as noted in the experimental part.

In view of the moderate overall yields and the availability of each starting material, this method using the Mannich reaction would be useful for the preparation of 3- and 4-alkylaminomethylpyridazines.

Experimental[7]

3-Hydroxy-6-alkylaminomethylpyridazine 1-Oxide Hydrochlorides (IIIa—e)——A typical experiment for these hydrochlorides is described with IIIa.

3-Hydroxy-6-dimethylaminomethylpyridazine 1-Oxide Hydrochloride (IIIa): To a suspended solution of 2.24 g (0.02 mole) of 3-hydroxypyridazine 1-oxide (II) in 15 ml of ethanol was added dropwise a solution of 2.18 g (0.023 mole) of 37% formalin and 2.51 g (0.023 mole) of a 40% dimethylamine solution in 20 ml of ethanol with stirring under ice cooling. The reaction mixture was allowed to stand for overnight, evaporated under reduced pressure, and the residue was recrystallized from ethanol to give yellowish granules, mp 178° (decomp.). Yield, 1.38 g (82%). *Anal.* Calcd. for $C_7H_{11}O_2N_3 \cdot C_4H_4O_2N_2$: C, 46.97; H, 5.38; N, 24.90. Found: C, 46.78; H, 5.56; N, 25.25. This salt was dissolved in a small amount of water, the solution was acidified with 10% hydrochloric acid, and the precipitated II (0.60 g) was filtered. The filtrate was concentrated under reduced pressure, and the residue was recrystallized from ethanol. IIIa: Colorless leaflets, mp 229—230°. Yield, 2.26 g (75%). *Anal.* Calcd. for $C_7H_{11}O_2N_3 \cdot HCl$: C, 40.88; H, 5.88; N, 20.43. Found: C, 40.82; H, 5.84; N, 20.84.

3-Hydroxy-6-dibenzylaminomethylpyridazine 1-Oxide Hydrochloride (IIIb): Colorless needles (from methanol), mp 210° (decomp.). Yield, 74%. *Anal.* Calcd. for $C_{19}H_{19}O_2N_3 \cdot HCl$: C, 63.80; H, 5.64; N, 11.75. Found: C, 63.78; H, 5.67; N, 11.73.

7) All melting points are uncorrected. Infrared spectra were measured on a JASCO Model-IR infrared spectrophotometer. NMR spectra were determined on a Japan Electron Optics Model C-6H spectrometer.

3-Hydroxy-6-pyrrolidinomethylpyridazine 1-Oxide Hydrochloride (IIIc): Colorless, fine needles (from ethanol), mp 201—203°. Yield, 52%. *Anal.* Calcd. for $C_9H_{13}O_2N_2 \cdot HCl$: C, 46.57; H, 6.09; N, 18.22. Found: C, 46.10; H, 6.07; N, 17.95.

3-Hydroxy-6-morpholinomethylpyridazine 1-Oxide Hydrochloride (IIId): Colorless pillars (ethanol), mp 211° (decomp.). Yield, 68%. *Anal.* Calcd. for $C_9H_{13}O_2N_3 \cdot HCl$: C, 46.92; H, 5.23; N, 18.14. Found: C, 46.52; H, 5.13; N, 17.83.

3-Hydroxy-6-(4-methylpiperidinomethyl)pyridazine 1-Oxide Hydrochloride (IIIe): Colorless needles (from a mixture of methanol and ethanol), mp 229° (decomp.). Yield, 81%. *Anal.* Calcd. for $C_{11}H_{17}O_2N_3 \cdot HCl$: C, 50.88; H, 6.98; N, 16.19. Found: C, 50.53; H, 6.93; N, 16.30.

6-Alkylaminomethyl-3(2H)-pyridazinones (IVa—e)——A typical experiment for IVa—e is described with IVe.

6-Dimethylaminomethyl-3(2H)-pyridazinone (IVa): Hydrochloride, colorless scales (from ethanol), mp 259—261° (decomp.). Free base,[6a] colorless leaflets (from diisopropyl ether), mp 104—105°. Yield, 94%.

6-Benzylaminomethyl-3(2H)-pyridazinone (IVb): Hydrochloride, colorless granules (from methanol), mp 225° (decomp.). Yield, 89%. *Anal.* Calcd. for $C_{12}H_{13}ON_3 \cdot HCl$: C, 55.28; H, 5.73; N, 16.12. Found: C, 54.81; H, 5.48; N, 15.93. Free base, pale yellow needles (from a mixture of ethanol and diisopropyl ether), mp 144—145°.

6-Pyrrolidinomethyl-3(2H)-pyridazinone (IVc): Hydrochloride, colorless granules (from ethanol), mp 228—230° (decomp.). Free base, colorless leaflets (from ethyl acetate), mp 136—137°. Yield, 91%. *Anal.* Calcd. for $C_9H_{13}ON_3$: C, 60.31; H, 7.31; N, 23.45. Found: C, 60.29; H, 7.57; N, 24.08.

6-Morpholinomethyl-3(2H)-pyridazinone (IVd): Colorless leaflets[6a] (from diisopropyl ether), mp 147—148°. Yield, 95%.

6-(4-Methylpiperidinomethyl)-3(2H)-pyridazinone (IVe): A solution of 5.19 g (0.02 mole) of IIIe in 100 ml of methanol was submitted to catalytic deoxidation over a catalyst prepared from 25 ml of a 1% palladium chloride solution and 0.4 g of charcoal. After one molar equivalent of hydrogen was absorbed, the catalyst was removed by filtration. The filtrate was evaporated, and the residue was recrystallized from a mixture of methanol and ethanol to give colorless leaflets, mp 274° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 2460 (=NH+-), 1690 (CO). Yield, 4.52 g (93%). *Anal.* Calcd. for $C_{11}H_{17}ON_3 \cdot HCl$: C, 54.20; H, 7.44; N, 17.21. Found: C, 54.44; H, 7.55; N, 17.38. The free base was prepared as follows. The hydrochloride was dissolved in a small amount of water, the solution was made alkaline with sodium bicarbonate, and extracted with chloroform repeatedly. After treatment with anhyd. sodium sulfate, the chloroform was evaporated on a water bath, and the residue was recrystallized from diisopropyl ether to give colorless leaflets, mp 125—127°. *Anal.* Calcd. for $C_{11}H_{17}ON_3$: C, 63.74; H, 8.27; N, 20.27. Found: C, 63.70; H, 8.01; N, 20.18.

3-Chloro-6-alkylaminomethylpyridazine (Va—e)——Since Va and Vb were directly submitted to catalytic dehalogenation without isolation, a typical experiment was described with Ve.

3-Chloro-6-pyrrolidinomethylpyridazine (Vc): Colorless needles (from diisopropyl ether), mp 51—54°. Yield, 68%. NMR τ ($CDCl_3$): 5.95 (s, CH_2), 2.45, 2.24 (a pair of doublet due to H^4 and H^5, J=6.0 Hz). *Anal.* Calcd. for $C_9H_{12}N_3Cl$: C, 54.68; H, 6.10; N, 21.26. Found: C, 54.76; H, 6.28; N, 21.37.

3-Chloro-6-morpholinomethylpyridazine (Vd): Yellowish pillars (from a mixture of methanol and diisopropyl ether), mp 115—116°. Yield, 72%. *Anal.* Calcd. for $C_9H_{12}ON_3Cl$: C, 50.59; H, 5.66; N, 19.67. Found: C, 50.82; H, 5.69; N, 19.60.

3-Chloro-6-(4-methylpiperidinomethyl)pyridazine (Ve): A mixture of 2.07 g (0.01 mole) of IVe and 30 ml of phosphorus oxychloride was refluxed for 30 min, and the excess phosphorus oxychloride was distilled off under reduced pressure. The residue was treated with cracked ice, the resulting solution was neutralized with sodium carbonate under ice-cooling, and extracted with chloroform. After treatment with sodium sulfate, the chloroform layer was shaked with a small amount of alumina in order to absorb the tar produced. After separation of the alumina by filtration, the chloroform was evaporated to dryness, and the residue was recrystallized from diisopropyl ether to give colorless needles, mp 104—105°. NMR τ ($CDCl_3$): 6.14 (s, CH_2), 2.48, 2.20 (a pair of doublet due to H^4 and H^5, J=6.0 Hz). Yield, 1.50 g (66%). *Anal.* Calcd. for $C_{11}H_{16}N_3Cl$: C, 58.53; H, 7.14; N, 18.62. Found: C, 58.30; H, 6.84; N, 18.82.

3-Alkylaminomethylpyridazines (VIa—e)——A typical experiment is described with VIa.

3-Dimethylaminomethylpyridazine (VIa): A solution of 1.72 g (0.01 mole) of Va in 30 ml of methanol was submitted to catalytic dehalogenation over a catalyst prepared from 10 ml of a 1% palladium chloride solution and 0.4 g of charcoal. After one molar equivalent of hydrogen was absorbed, the catalyst was removed by filtration. The residue was made alkaline with a 20% sodium hydroxide solution, and the oil separated was extracted with chloroform. The chloroform layer was washed with water, dried over anhyd. sodium sulfate, and the chloroform was evaporated to dryness. The residue was distilled under reduced pressure, bp 76—78°/2 mmHg. Yield, 0.96 g (70%). NMR τ ($CDCl_3$): 7.64 (s, Me_2N), 6.14 (s, CH_2). Oxalate: Colorless leaflets (from ethanol), mp 158—159° (decomp.). *Anal.* Calcd. for $C_7H_{11}N_3 \cdot C_2H_2O_4$: C, 47.57; H, 5.77; N, 18.49. Found: C, 47.75; H, 5.90; N, 18.89. Picrate: Yellow needles (from ethanol), mp 133—135°. *Anal.* Calcd. for $C_7H_{11}N_3 \cdot C_6H_3O_7N_3$: C, 42.64; H, 3.85; N, 22.95. Found: C, 42.64; H, 3.95; N, 23.06.

3-Benzylaminomethylpyridazine (VIb): Colorless oil. Oxalate, pale yellow leaflets (from ethanol), mp 197° (decomp.). Yield, 89%. *Anal.* Calcd. for $C_{12}H_{13}N_3 \cdot C_2H_2O_4$: C, 58.12; H, 5.23; N, 14.45. Found: C, 58.10; H, 5.23; N, 13.47.

3-Pyrrolidinomethylpyridazine (VIc): Colorless oil, 85—87°/2 mmHg. Yield, 48%. Picrate: Yellow needles (from ethanol), mp 149°. *Anal.* Calcd. for $C_9H_{13}N_3 \cdot 2C_6H_{13}O_7N_3$: C, 40.59; H, 3.08; N, 20.27. Found: C, 40.56; H, 3.19; N, 20.50.

3-Morpholinomethylpyridazine (VId): Pale yellow needles (from diisopropyl ether), mp 52—54°. Yield, 78%. Picrate: Yellow needles (from ethanol), mp 167° (decomp.). *Anal.* Calcd. for $C_9H_{13}ON_3 \cdot 2C_6H_{13}O_7N_3$: C, 39.57; H, 3.01; N, 19.78. Found: C, 39.53; H, 3.03; N, 19.24.

3-(4-Methylpiperidinomethyl)pyridazine (VIe): Colorless needles (from diisopropyl ether), mp 74—76°, bp 104—107°/2 mmHg. Yield, 82%. *Anal.* Calcd. for $C_{11}H_{17}N_3$: C, 69.07; H, 8.96; N, 21.97. Found: C, 68.33; H, 8.68; N, 22.58. Oxalate: Colorless needles (from ethanol), mp 154—156° (decomp.). *Anal.* Calcd. for $C_{11}H_{17}N_3 \cdot C_2H_2O_4$: C, 55.50; H, 6.81; N, 14.94. Found: C, 55.72; H, 6.83; N, 15.16.

3-Ethoxy-6-alkylaminomethylpyridazines (VIIc, VIIe)——3-Ethoxy-6-pyrrolidinomethylpyridazine (VIIc): To a solution of 0.23 g (0.01 mole) of metallic sodium in 10 ml of abs. ethanol was added a solution of 1.98 g (0.01 mole) of Vc in 10 ml of abs. ethanol, and the mixture was refluxed on a water bath for 30 min. The reaction mixture was evaporated to dryness, the residue was extracted with chloroform, and the chloroform solution was passed through an alumina column. The chloroform eluant was evaporated, and the residue was distilled under reduced pressure, bp 131—133°/12 mmHg. Yield, 1.62 g (78%). Picrate: Yellow plates (from ethanol), mp 128—130°. *Anal.* Calcd. for $C_{11}H_{17}ON_3 \cdot C_6H_3O_7N_3$: C, 46.79; H, 4.62; N, 19.26. Found: C, 46.55; H, 4.63; N, 19.64.

3-Ethoxy-6-(4-methylpiperidinomethyl)pyridazine (VIIe) was similarly prepared from Ve. Colorless needles (from pet. ether), mp 76—77°. Yield, 86%. *Anal.* Calcd. for $C_{13}H_{21}ON_3$: C, 66.35; H, 9.00; N, 17.86. Found: C, 66.25; H, 8.98; N, 17.75.

4-Alkylaminomethylpyridazines (XIVa, XIVb)——Since some of 3-hydroxy-4-alkylaminomethyl-6-chloropyridazine 1-oxides and 4-alkylaminomethyl-3(2H)-pyridazinones were already reported in our previous paper,[6b] the data of new compounds were noted here.

3-Chloro-4-morpholinomethylpyridazine (XIa): A mixture of 1.95 g (0.01 mole) of Xa and 25 ml of phosphorus oxychloride was heated on a boiling water bath for 1 hr. The excess phosphorus oxychloride was distilled off under reduced pressure, the residue was treated with cracked ice, the dark brown solution was neutralized with sodium bicarbonate, and the slightly alkaline solution was extracted with ether. After treatment with anhyd. sodium sulfate, the ether was evaporated, and the residue was recrystallized from diisopropyl ether to give orange needles, mp 102—104°. NMR τ ($CDCl_3$): 6.31 (s, CH_2), 2.20, 0.76 (a pair of doublet due to H^5 and H^6, $J=4.0$ Hz). Yield, 1.36 g (64%). *Anal.* Calcd. for $C_9H_{12}ON_3Cl$: C, 50.54; H, 5.66; N, 19.67. Found: C, 50.82; H, 5.47; N, 19.58. Oxalate: Orange granules (from ethanol), mp 121—123° (decomp.). *Anal.* Calcd. for $C_9H_{12}ON_3Cl \cdot C_2H_2O$: C, 49.07; H, 5.62; N, 15.61. Found: C, 49.21; H, 5.61; N, 15.41.

4-Morpholinomethylpyridazine (XIIa): A mixture of 0.43 g (0.002 mole) of XIa and 0.4 ml of conc. ammonia in 30 ml of methanol was submitted to catalytic dehalogenation over a catalyst prepared from 20 ml of a 1% palladium chloride solution and 0.2 g of charcoal. When one molar equivalent of hydrogen was absorbed, the hydrogenation was stopped, and the catalyst was filtered off. The filtrate was evaporated to dryness, the residue was extracted with ether, and the ether was distilled off. Colorless oil. Yield, 1.28 g (71%). Oxalate: Pale brownish granules (from ethanol), mp 147° (decomp.). *Anal.* Calcd. for $C_9H_{13}ON_3 \cdot C_2H_2O_4$: C, 49.07; H, 5.62; N, 15.61. Found: C, 49.21; H, 5.61; N, 15.68. Picrate: Brownish leaflets (from ethanol), mp 168—169° (decomp.). *Anal.* Calcd. for $C_9H_{13}ON_3 \cdot 2C_6H_3O_7N_3$: C, 39.57; H, 3.00; N, 19.86. Found: C, 39.91; H, 3.02; N, 19.49.

3-Chloro-4-piperidinomethylpyridazine (XIb) and 4-piperidinomethylpyridazine (XIIb) were analogously synthesized. Their physical and analytical data were described bellow.

3-Chloro-4-piperidinomethylpyridazine (XIb): Colorless leaflets (from diisopropyl ether), mp 58—60°, bp 150°/7 mmHg. NMR τ ($CDCl_3$): 6.42 (s, CH_2), 2.10, 0.24 (a pair of doublet due to H^5 and H^6, $J=4.0$ Hz). Oxalate: Colorless pillars (from ethanol), mp 139° (decomp.). *Anal.* Calcd. for $C_{10}H_{14}N_3Cl \cdot C_2H_2O_4$: C, 47.76; H, 5.32; N, 13.92. Found: C, 47.46; H, 5.53; N, 13.82.

4-Piperidinomethylpyridazine (XIIb): Colorless oil, bp 125—130°/1 mmHg (bath temperature). *Anal.* Calcd. for $C_{10}H_{15}N_3$: C, 67.76; H, 8.53; N, 23.71. Found: C, 67.51; H, 8.42; N, 23.34.

When catalytically hydrogenated over palladium-on-charcoal, XIIb gave 4-methylpyridazine in 92% yield. 4-Methylpyridazine oxalate: Brownish granules (from ethanol), mp 114—116°.

3,5-Bis(morpholinomethyl)pyridazine (XVI)——3-Hydroxy-4,6-bis(morpholinomethyl) pyridazine 1-oxide (XIII) and 4,6-bis(morpholinomethyl)-3(2H)-pyridazinone (XIV) were already reported in our previous paper.[6b]

3-Chloro-4,6-bis(morpholinomethyl)pyridazine (XV): A mixture of 1.47 g (0.005 mole) of XIV and 20 ml of phosphorus oxychloride was refluxed for 30 min. The reaction mixture was poured into ice-water, made alkaline with sodium carbonate, and the solution was extracted with chloroform. The combined extract was dried over anhyd. sodium sulfate, the chloroform was evaporated to dryness, and the residue was recrys-

tallized from diisopropyl ether. Colorless plates, mp 100—101°. Yield, 1.28 g (82%). NMR τ ($CDCl_3$): 2.30 (s, H^5), 6.18 (s, 6-CH_2), 6.27 (s, 4-CH_2). *Anal.* Calcd. for $C_{14}H_{21}O_2N_4Cl$: C, 53.75; H, 6.77; N, 17.91. Found: C, 53.87; H, 6.94; N, 17.70.

3,5-Bis(morpholinomethyl)pyridazine (XVI): A solution of 0.56 g (0.0018 mole) of XV in 25 ml of ethanol was submitted to catalytic dehalogenation using a catalyst prepared from 15 ml of a 1% palladium chloride and 0.2 g of charcoal. During five hours, 40 ml of hydrogen was absorbed, the catalyst was filtered off, and the methanol was evaporated to dryness. The residue was dissolved in a small amount of water, the solution was made alkaline with a 10% sodium hydroxide solution, and the alkaline solution was extracted with chloroform. The chloroform was evaporated to dryness and the residue was distilled under reduced pressure to give yellowish viscous oil, bp 210—214°/2 mmHg, which solidified on standing. mp 60—62°. Yield, 0.42 g (82%). NMR τ (DMSO-d_6): 1.05 (d, H^3, J=1.5 Hz), 2.48 (d, H^5, J=1.5 Hz), 4.24 (s, 4-CH_2), 4.75 (s, 6-CH_2). Oxalate: Colorless granules (from ethanol), mp 136—137° (decomp.). *Anal.* Calcd. for $C_{14}H_{22}O_2N_4 \cdot 2C_2H_2O_4$: C, 47.16; H, 5.72; N, 12.22. Found: C, 46.80, H, 5.79; N, 12.12.