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180. Takanobu Itai and Shozo Kamiya : Potential Anti-cancer Agents. XI.*1 Synthesis of 4- and 5-Azidopyridazine 1-Oxide.

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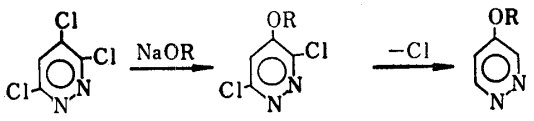
Previously, the authors synthesized 3- and 6-azidopyridazine 1-oxide derivatives, and the reactions of azido groups in these compounds were examined.

In the present paper, synthesis and reaction of 4- and 5-azidopyridazine 1-oxide will be described.

Synthesis of 4- and 5-Azidopyridazine 1-Oxide

Reaction of 3,4,6-trichloropyridazine (I) with an equimolar amount of sodium alkoxide was recently reported by Eichenberger[1a] and Kuraishi[1b] to yield 4-alkoxy-3,6-dichloropyridazine (II), which was converted to 4-alkoxypyridazine (III) by catalytic dehalogenation.



I II III

First, we examined the substitution reaction of easily obtainable 3,4,5-trichloropyridazine[2] (IV) in order to synthesize the starting material, 4-methoxypyridazine (X).

When 3,4,5-trichloropyridazine (IV) was treated with an equimolar amount of sodium methoxide with cooling, then refluxing on a water bath, a monomethoxy-dichloropyridazine (V) was formed in 38% yield and the remainder was an uncrystallizable substance. V was quantitatively converted to 4-methoxypyridazine (X) by catalytic hydrogenation over palladium-charcoal. The monomethoxy-dichloropyridazine (V) was heated with a second equimolar amount of sodium methoxide. From the reaction mixture, two kinds of dimethoxy-monochloropyridazine were obtained, VI, m.p. 161° in 38% and VII, m.p. 91° in 24% yield. One of the dimethoxy-monochloropyridazine, VI was dehalogenated to a dimethoxypyridazine (VIII), m.p. 73~75°, which was identical with 3,5-dimethoxypyridazine,[3] previously synthesized by S. Natsume. Another dimethoxypyridazine (IX), m.p. 98°, derived from VII was different from 3,4-dimethoxypyridazine.[4] From these facts, VI should be 4-chloro-3,5-dimethoxypyridazine and VII may be considered as 3-chloro-4,5-dimethoxypyridazine. Consequently, V was determined as 5-methoxy-3,4-dichloropyridazine. The reaction of IV with two equimolar amounts of sodium methoxide resulted in the formation of VI in 25% and VII in 41% yields. However, 3,4,5-trimethoxypyridazine was not produced by heating VI and VII with sodium methoxide at 130°, recovering most of the starting material.

Itai and Natsume[4] recently reported the N-oxidation of 4-methoxypyridazine (X) with 30% hydrogen peroxide solution in acetic acid. In the present work, X was left

*1 Part X : This Bulletin, **11**, 348 (1963).

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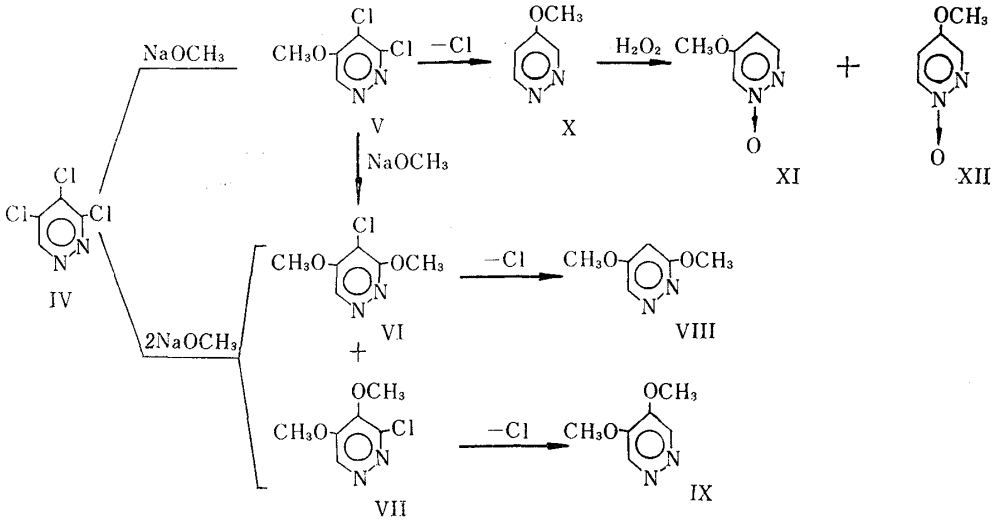
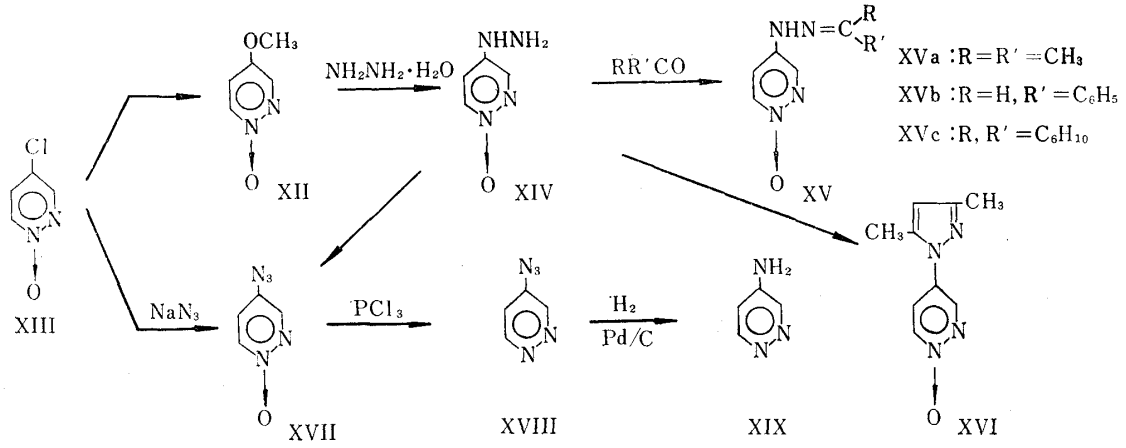
1) *a*) K. Eichenberger, R. Rometsch, J. Druey : Helv. Chim. Acta, **39**, 1755 (1956). *b*) T. Kuraishi: This Bulletin, **5**, 376 (1957).
2) T. Kuraishi : This Bulletin, **4**, 497 (1956).
3) T. Itai, S. Natsume : *Ibid.*, to be published.
4) *Idem* : *Ibid.*, **10**, 643 (1962).



for ten days at room temperature with 60% hydrogen peroxide solution. From the reaction mixture, 1-methyl-4(1*H*)-pyridazinone[1a] in 30~40% yield, as a main product, 2-oxide (XI) in 13%, and 1-oxide (XII) in 7% were obtained.

When 4-methoxypyridazine 1-oxide (XII) was treated with alcoholic hydrazine hydrate, 4-hydrazinopyridazine 1-oxide (XIV) was produced in 43% yield, forming black pillars, m.p. 192~193° (decomp.), and the treatment of XIV with carbonyl compounds, such as acetone, benzaldehyde, or cyclohexanone gave corresponding hydrazones (XVa, XVb, XVc).



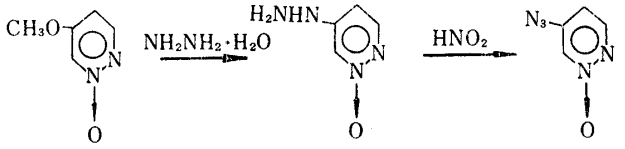
Fischer's indole synthesis was attempted by heating 4-(2-cyclohexylidenehydrazino)-pyridazine 1-oxide (XVc) in a mixture of sulfuric acid and acetic acid to obtain a pyridazo-indole derivative, but most of the starting material was recovered.

The hydrazino group of XIV could easily cyclize with acetylacetone to give 4-(3,5-dimethyl-1-pyrazolyl)pyridazine 1-oxide (XVI).

4-Azidopyridazine 1-oxide (XVII) was produced in 48% yield on the treatment of XIV with nitrous acid. XVII obtained here was sensitive to light, just like 4-azidopyridine (or quinoline) 1-oxide.[5a,b] 4-Azidopyridazine (XVIII) was obtained by refluxing XVII with phosphorus trichloride in chloroform and the catalytic hydrogenation of XVIII over palladium-charcoal gave 4-aminopyridazine[6] (XIX) quantitatively, which was identical with the authentic sample.

5) *a*) T. Itai, S. Kamiya: This Bulletin, **9**, 87 (1961). *b*) S. Kamiya: *Ibid.*, **10**, 471 (1962).
6) T. Kuraishi: *Ibid.*, **4**, 497 (1956).

In our previous paper,[5a] we reported that ionic reaction of 4-chloropyridine 1-oxide with sodium azide in hydrated alcohol, at 180° for 8 hours in a sealed tube, afforded only 10% of 4-azidopyridine 1-oxide and that most of the starting material was recovered. However, the same reaction of 4-chloropyridazine 1-oxide (XIII) under a milder condition (100°, 5 hours in a sealed tube) gave 51% yield of 4-azidopyridazine 1-oxide (XVII). In this reaction, 4-aminopyridazine 1-oxide was isolated in 4% yield. It was found that the chlorine atom in 4-position of pyridazine 1-oxide was more reactive than that in pyridine 1-oxide with sodium azide.



Synthesis of 5-azidopyridazine 1-oxide (XXI) was similarly accomplished by the treatment of XI with alcoholic hydrazine hydrate to form 5-hydrazinopyridazine 1-oxide (XX) in 30% yield, followed by the treatment of XX with nitrous acid in 70% yield, forming slightly yellow crystals, m.p. 102° (decomp.), insensitive to light. The treatment of XX with benzaldehyde gave 5-(2-benzylidenehydrazino)pyridazine 1-oxide.

Reaction of 4- and 5-Azidopyridazine 1-Oxide

It is well known that the N-oxide group of pyridine (or quinoline) 1-oxide derivative has generally increased polar effect in their nitrogens and the reactivity of 2- and 4-positions is further potentiated. Actually, the 4-azido group activated by the N-oxide group,[5b] N-alkyl, or N-alkoxyammonium group[7] is so reactive that it is replaced easily by an ionic reaction and more easily decomposed to form the corresponding azo or amino compounds by radical reaction.

On the contrary, it was considered that the azido group of 3-azidopyridine (or quinoline) 1-oxide[8] (XXII) should hardly be affected by the polar effect of its N-oxide group. Actually, XXII and 4-azidoquinoline were quite inactive, most of the starting material being recovered on the reaction with sodium alkoxide or on thermal decomposition.

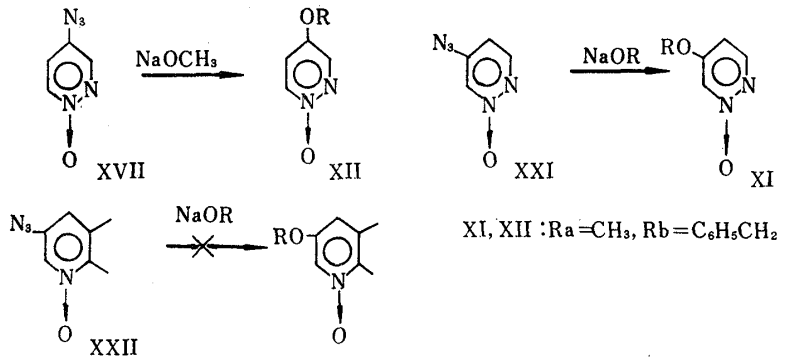
In radical reaction of 4-azidopyridazine 1-oxide (XVII), it was unquestionable that the azido group of XVII behaved as that of 4-position activated by N-oxide group and was susceptible to radical cleavage as expected. Actually, XVII was sensitive to light and easily decomposed to an azo compound on exposure to sunlight in a solution. On the other hand, 5-azidopyridazine 1-oxide (XXI) was quite stable on exposure to sunlight, just like 3-azidopyridine 1-oxide (XXII).

In ionic reaction with sodium alkoxides, XVII gave 4-alkoxypyridazine 1-oxide (XIIa, XIIb) as expected, either by standing the mixture at room temperature overnight or by heating on a water bath. However, in the case of 5-azidopyridazine 1-oxide (XXI), structually similar to XXII, ionic reaction also took place under the same condition as for XVII, and 5-alkoxypyridazine 1-oxide (XIa, XIb) was produced in a good yield. In this case, the polar effect of nitrogen at 2-position cannot be overlooked.

From the results hereby obtained, ionic reactivity of these azido groups at 3-, 4-, 5-, and 6-positions could not be differentiated. These reactivities must be examined again, preferrably by a kinetic method.

The derivatives prepared in the present work have been submitted for biological test, the result of which will be reported separately.

7) S. Kamiya: This Bulletin, **10**, 669 (1962).
8) *Idem*: Yakugaku Zasshi, **81**, 1743 (1961).



Experimental*3

5-Methoxy-3,4-dichloropyridazine (V)——To a solution of 0.61 g. of metallic Na dissolved in 50 ml. of anhyd. MeOH, 4.88 g. of 3,4,5-trichloropyridazine was added under ice cooling. The reaction mixture was allowed to stand for 1 hr. at 0° to 5° and then at room temperature for 3 hr. After refluxing on a water bath for 1 hr., NaCl that precipitated out was filtered off and the filtrate was concentrated to about 30 ml. A considerable amount of H_2O was added to the filtrate till white fine needles deposited. The needles were collected by suction, washed with ice-H_2O and dried in a reduced desiccator. Recrystallization from hyd. EtOH gave white needles, m.p. 101～102°. Yield, 1.60 g. (37%). *Anal.* Calcd. for $C_5H_4ON_2Cl_2$: C, 33.55; H, 2.26. Found: C, 33.80; H, 2.60.

4-Methoxypyridazine (X) from 5-Methoxy-3,4-dichloropyridazine (V)——A solution of 1.0 g. of V dissolved in 20 ml. of MeOH, added with a catalyst prepared from 20 ml. of 1% $PdCl_2$ solution and 0.5 g. of charcoal, and 10 ml. of conc. NH_4OH, was submitted to dehalogenation. After two moles of H_2 was absorbed, the catalyst was filtered off, washed with MeOH and the filtrate was evaporated. The residue was extracted with $CHCl_3$, dried over anhyd. K_2CO_3, the solvent was evaporated to dryness, and the residue was allowed to stand in a desiccator, by which it solidified. Very hygroscopic needles. Picrate: Yellow needles, m.p. 143～144°. This, on admixture with an authentic sample, gave no melting point depression. Yield, quantitative.

Reaction of 5-Methoxy-3,4-dichloropyridazine (V) with MeONa——To a solution of 0.18 g. of metallic Na dissolved in 20 ml. of anhyd. MeOH, 1.40 g. of V was added and the solution was refluxed on a water bath for 3 hr. MeOH was evaporated to dryness, the residue was extracted with $CHCl_3$, and $CHCl_3$ was evaporated to dryness. Yield, 1.26 g. The residue was separated by fractional crystallization from MeOH to white needles, m.p. 159～160°. This filtrate was concentrated again to yield a second crop of crystals, m.p. 155～157°. These two products were 4-chloro-3,5-dimetoxypyridazine (VI) and recrystallized again from MeOH to colorless needles, m.p. 161～162°. *Anal.* Calcd. for $C_6H_7O_2N_2Cl$: C, 41.27; H, 4.04. Found: C, 41.42; H, 3.84. Yield, 0.57 g. (38%).

The second filtrate was concentrated, the deposited crystals were collected by suction, and recrystallized from MeOH to m.p. 91～92°. *Anal.* Calcd. for $C_6H_7O_2N_2Cl$: C, 41.27; H, 4.04. Found: C, 41.09; H, 4.04. This was 3-chloro-4,5-dimethoxypyridazine (VII). Yield, 0.36 g. (24%).

VI was dehalogenated by catalytic hydrogenation in the presence of conc. NH_4OH to yield 3,5-dimethoxypyridazine,[3] colorless needles (from a mixture of benzene and petr. benzin), m.p. 73～75°, in 74% yield. VII was similarly dehalogenated to 4,5-dimethoxypyridazine, hygroscopic colorless pillars (from benzene), m.p. 98～100°. *Anal.* Calcd. for $C_6H_8O_2N_2 \cdot H_2O$: C, 45.56; H, 6.37. Found: C, 45.85; H, 6.38. Picrate: Yellow needles, m.p. 165°(from EtOH). *Anal.* Calcd. for $C_6H_8O_2N_2 \cdot C_6H_3O_7N_3$: C, 39.03; H, 3.00. Found: C, 39.30; H, 3.34.

Reaction of 3,4,5-Trichloropyridazine (IV) with Two Equimolar Amounts of MeONa——To a solution of 1.31 g. of metallic Na dissolved in anhyd. MeOH, 5.22 g. of IV was added, the mixture was allowed to stand for 3 hr. at room temperature, and then refluxed on a water bath for 1.5 hr. NaCl that separated out was filtered off, the filtrate was evaporated to dryness, and the residue was extracted with $CHCl_3$. $CHCl_3$ was evaporated and the residue was separated by fractional crystallization with MeOH to colorless needles, m.p. 160～162°. This product was identical with 4-chloro-3,5-dimethoxypyridazine. Yield, 1.22 g. (25%). The second filtrate was concentrated, and the deposited colorless needles, were collected and recrystallized from benzene to colorless needles, m.p. 89～90°. This, on admixture with 3-chloro-4,5-dimethoxypridazine, gave no melting point depression. Yield, 2.12 g. (41%).

4-Methoxypyridazine 1-Oxide (XII) from 4-Chloropyridazine 1-Oxide (XIII)——To a solution of MeONa, prepared by adding 0.19 g. of metallic Na to 40 ml. of anhyd. MeOH, was added 1.042 g. of XIII and the

*3 All melting points are uncorrected.

mixture was heated for 2 hr. on a water bath. MeOH was evaporated to dryness, the residue was extracted with $CHCl_3$ and dried over anhyd. Na_2SO_4. $CHCl_3$ was evaporated and the residue was recrystallized from a mixture of benzene and petr. benzin, White leaflets, m.p. 124~125°. This on admixture with 4-methoxypyridazine 1-oxide, gave no melting-point depression. Yield, 0.97 g. (96%).

4-Hydrazinopyridazine 1-Oxide (XIV) from 4-Methoxypyridazine 1-Oxide (XII)——A mixture of 0.97 g. of XII, 5.0 ml. of 80% $NH_2NH_2 \cdot H_2O$, and 5 ml. of EtOH was refluxed on a water bath for 3 hr. The reaction mixture was evaporated to dryness in a reduced pressure and the yellow residue was recrystallized from a mixture of MeOH and EtOH to black pillars, m.p. 192~193°(decomp.). *Anal.* Calcd. for $C_4H_6ON_4$: C, 38.09; H, 4.80. Found: C, 38.28; H, 5.44. Yield, 0.42 g. (43%).

1) 4-(2-Benzylidenehydrazino)pyridazine 1-Oxide (XVa): Pale brownish fine dices (from EtOH), m.p. 252° (decomp.). *Anal.* Calcd. for $C_{11}H_{10}ON_4$: C, 61.67; H, 4.71. Found: C, 61.64; H, 4.96.

2) 4-(2-Isopropylidenehydrazino)pyridazine 1-Oxide (XVb): Slightly brownish needles (from a mixture of EtOH and petr. benzin), m.p, 218°. *Anal.* Calcd. for $C_7H_{10}ON_4$: C, 50.59; H, 6.06. Found: C, 50.67; H, 6.13.

3) 4-(2-Cyclohexylidenhydrazino)pyridazine 1-Oxide (XVc): A mixture of 0.50 g. of XIV, 1.0 g. of cyclohexanone, and 10 ml. of EtOH was refluxed on a water bath for 2 hr. The reaction mixture was evaporated to dryness under reduced pressure, and the residue was allowed to stand in a desiccator, by which it solidified. Recrystallization from EtOH gave pale yellow dices, m.p. 196~199°. *Anal.* Calcd. for $C_{10}H_{14}ON_4$: C, 58.23; H, 6.84. Found: C, 58.76; H, 6.48. Yield, quantitative.

4-Azidopyridazine 1-Oxide (XVII)——1) Reaction of 4-Hydrazinopyridazine 1-Oxide (XIV) and HNO_2: To a solution of 0.10 g. of XIV dissolved in 5 ml. of 5% HCl, a solution of 55 mg. of $NaNO_2$ dissolved in 2 ml. of H_2O was added dropwise under cooling. After standing for 20 min., the reaction mixture was basified with $NaHCO_3$, and extracted with $CHCl_3$. After drying over anhyd. Na_2SO_4, the solvent was evaporated to dryness. Recrystallization from benzene gave needles, m.p. 123°(decomp.). UV: $\lambda_{max}^{95\%\ EtOH}$ 293 mμ (log ε 4.24). IR ν_{max}^{Nujol} cm^{-1}: 2120, 2140 (N_3). *Anal.* Calcd. for $C_4H_3ON_5$: C, 35.04; H, 2.21. Found: C, 35.33; H, 2.58. Yield, 52 mg. (48%).

2) Reaction of 4-Chloropyridazine 1-Oxide (XIII) and NaN_3: A mixture of 0.60 g. of XIII, 0.60 g. of NaN_3, 2 ml. of H_2O, and 8 ml. of EtOH was heated in a sealed tube in a boiling water bath for 5 hr. After cooling, the reaction mixture was evaporated to dryness under reduced pressure and the residue was extracted with $CHCl_3$. After drying over anhyd. Na_2SO_4, the solvent was evaporated. Recrystallization from a mixture of benzene and petr. ether gave straw yellow needles, m.p. 123~124°(decomp.). This, on admixture with 4-azidopyridazine 1-oxide, gave no melting point depression. Yield, 0.32 g. (51%). The aqueous layer extracted off with $CHCl_3$ was evaporated to dryness under reduced pressure. The residue was allowed to stand in a reduced desiccator overnight, extracted with hot AcOEt, and the extract was concentrated, leaving pale yellow needles. The IR spectrum of this product was identical with of 4-aminopyridazine 1-oxide.[4] Yield, 21 mg. (4%).

4-Azidopyridazine (XVIII) from 4-Azidopyridazine 1-Oxide (XVII)——To a solution of 0.25 g. of XVII dissolved in 10 ml. of $CHCl_3$, 0.7 g. of PCl_3 was added, and the mixture was refluxed on a water bath for 2 hr. The reaction mixture was evaporated to dryness in a reduced pressure. After standing the residue with 5 ml. of ice H_2O, the solution was basified with $NaHCO_3$, extracted with $CHCl_3$, and the solvent was evaporated after drying over anhyd. Na_2SO_4. The residue was extracted again with $CHCl_3$, the solution was passed through an alumina column, and the column was eluted with $CHCl_3$. $CHCl_3$ was evaporated in a reduced pressure and the residue solidified. Unstable colorless prisms (from $CHCl_3$), m.p. 62~64°, sensitive to light. IR ν_{max}^{Nujol} cm^{-1}: 2090, 2190 (N_3). *Anal.* Calcd. for $C_4H_3N_5$: C, 39.67; H, 2.50. Found: C, 40.05; H, 2.57. Yield, 0.16 g. (70%).

4-Aminopyridazine (XIX) from 4-Azidopyridazine (XVIII)——A solution of 30 mg. of XVIII dissolved in 5 ml. of MeOH, added with a catalyst prepared from 8.4 ml. of 1% $PdCl_2$ solution and 0.2 g. of charcoal, was shaken in H_2 stream for 5 min. The catalyst was filtered off and washed with MeOH. MeOH-was evaporated to dryness and the residue was recrystallized from AcOEt to white needles, m.p. 129~130°, undepressed on admixture with the authentic sample.[6] Yield, quantitative.

4-(3,5-Dimethyl-1-pyrazolyl)pyridazine 1-Oxide (XVI) from 4-Hydrazinopyridazine 1-Oxide (XIV)——A solution of 0.20 g. of XIV, 0.24 g. of acetylacetone and 30 ml. of EtOH was refluxed on a water bath for 3 hr. The reaction mixture was evaporated to dryness under reduced pressure, and the residue was recrystallized from EtOH to white fine needles, m.p. 155~156°. *Anal.* Calcd. for $C_9H_{10}ON_4$: C, 56.83; H, 5.30. Found: C, 56.77; H, 5.46. Yield, 0.23 g. (76%).

5-Hydrazinopyridazine 1-Oxide (XX) from 5-Methoxypyridazine 1-Oxide (XI)——A mixture of 0.55 g. of XI, 5 ml. of EtOH and 2.5 ml. of 80% $NH_2NH_2 \cdot H_2O$ was refluxed on a water bath for 1 hr. The reaction mixture was evaporated to dryness in a reduced pressure, and the residue was recrystallized from EtOH to white needles, m.p. 188° (decomp.). *Anal.* Calcd. for $C_4H_6ON_4$: C, 38.09; H, 4.80. Found: C, 38.21; H, 4.69. Yield, 0.30 g. (55%).

5-(2-Benzylidenehydrazino)pyridazine 1-Oxide (XXII): Yellow fine crystals (from EtOH), m.p. 280° (decomp.). *Anal.* Calcd. for $C_{11}H_{10}ON_4$: C, 61.67; H, 4.71. Found: C, 61.80; H, 4.79.

5-Azidopyridazine 1-Oxide (XXI)——To a solution of 0.20 g. of 5-hydrazinopyridazine 1-oxide dissolved in 5 ml. of 5% HCl, a solution of 0.12 g. of $NaNO_2$ dissolved in 3 ml. of H_2O was added dropwise under cooling. After standing for 20 min., the reaction mixture was basified with $NaHCO_3$, and extracted with $CHCl_3$. After drying over anhyd. Na_2SO_4, the solvent was evaporated to dryness, and the residue was recrystallized from benzene to slightly pale yellow needles, m.p. 100~102°(decomp.). UV $\lambda_{max}^{95\%\ EtOH}$ mμ. (log ε): 254 (4.35), 313 (3.43). IR: ν_{max}^{Nujol} 2125 cm^{-1}(N_3). *Anal.* Calcd. for $C_4H_3ON_5$: C, 35.04; H, 2.21. Found: C, 35.56; H, 2.21. Yield, 0.16 g. (74%).

3-Azidopyridine 1-Oxide (XXII) from 3-Azidopyridine——A mixture of 3.10 g. of 3-azidopyridine prepared from 3-hydrazinopyridine[9] with HNO_2, 40 ml. of AcOH and 7.0 ml. of 30% H_2O_2 solution was heated at 75° for 3 hr., further 4.0 ml. of 30% H_2O_2 was added, and again heated at the same temperature for 3 hr. The reaction mixture was treated by the usual method. Slightly yellow leaflets (from benzene), m.p. 99~103°. IR: ν_{max}^{Nujol} 2120 cm^{-1}(N_3). *Anal.* Calcd. for $C_5H_4ON_4$: C, 44.12; H, 2.96. Found: C, 44.20; H, 3.21. Yield, 2.25 g. (64%).

Reaction of 3-Azidopyridine 1-Oxide (XXII) with MeONa——To a solution of 85 mg. of metallic Na dissolved in anhyd. MeOH, 0.50 g. of XXII was added, and the mixture was refluxed for 2 hr. on a water bath. MeOH was evaporated, and the residue was extracted with $CHCl_3$. After drying over anhyd. Na_2SO_4, $CHCl_3$ was distilled off, leaving straw yellow pillars, m.p. 100~101°, undepressed with 3-azidopyridine 1-oxide. 0.45 g. (90%).

Reaction of 4-Azidopyridazine 1-Oxide (XVII) with Sodium Alkoxides. Formation of 4-Alkoxypyridazine 1-Oxide (XIIa, XIIb)——1) MeONa. To a solution of 17 mg. of metallic Na dissolved in 10 ml. of anhyd. MeOH, 0.10 g. of XVII was added, and the mixture was refluxed on a water bath for 1 hr. MeOH was evaporated, the residue was extracted with hot $CHCl_3$ added a small amount of charcoal, and the solvent was evaporated. The residue was recrystallized from a mixture of benzene and petr. benzin to white leaflets, m.p. 124~125°. This, on admixture with 4-methoxypyridazine 1-oxide gave no melting point depression. Yield, 68 mg. (74%).

2) $C_6H_5CH_2ONa$. By the same treatment of XVII with $C_6H_5CH_2ONa$ as described in 1), 4-benzyloxypyridazine 1-oxide (XIIb), colorless leaflets (from benzene), m.p. 140~141° was obtained. *Anal.* Calcd. for $C_{11}H_{10}O_2N_2$: C, 65.33; H, 4.98. Found: C, 65.88; H, 5.19. Yield, 71%.

Reaction of 5-Azidopyridazine 1-Oxide (XXI) with Sodium Alkoxides. Formation of 5-Alkoxypyridazine 1-Oxide (XIa, XIb)——1) $C_6H_5CH_2ONa$. To a solution of 21 mg. of metallic Na dissolved in 5 ml. of anhyd. $C_6H_5CH_2OH$, 0.12 g. of XXI was added, and the mixture was heated on a water bath for 1 hr. NaN_3 precipitated out was filtered off and the filtrate was evaporated under reduced pressure. The residue was extracted with hot benzene, the solvent was concentrated, and a few drops of Et_2O was added after cooling. White prisms (from a mixture of benzene and Et_2O), m.p. 100~102°. *Anal.* Calcd. for $C_{11}H_{10}O_2N_2$: C, 65.33; H, 4.98. Found: C, 65.51; H, 5.14. Yield, 82 mg. (51%).

2) MeONa. Similarly, the treatment of XVI with MeONa gave 5-methoxypyridazine 1-oxide. Colorless prisms, m.p. 106~109°. Yield, 63%.

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Summary

Reaction of 3,4,5-trichloropyridazine (IV) with sodium methoxide was examined.

4-Azidopyridazine 1-oxide (XVII) and 5-azidopyridazine 1-oxide (XXI) were synthesized from corresponding hydrazino compounds (XIV, XX) with nitrous acid, and XVII was also derived from 4-chloropyridazine 1-oxide (XIII) with sodium azide.

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9) A. Binz, C. Räth: Ann., **486**, 95 (1931).