of 5α-spirostane-3β,12,20-triol 3-acetate. The reaction mixture was maintained at 60~65° for 2 hr., and solvent then removed under reduced pressure. The residue was extracted with CH_2Cl_2, washed with d. $NaHCO_3$ and dried. The organic phase was distilled and the residue crystallized from ether to give white needles (0.34 g., 43%), m.p. 217~219°. An analytical sample, recrystallized from MeOH, had m.p. 220~224.5°, $[\alpha]_D$ ±0°(c=0.9, EtOH). *Anal.* Calcd. for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found : C, 73.59; H, 8.91.

Acetylation to 3β,12β-Diacetate——The 12β-Hydroxyl group of Compound (Ⅶ) is considerably resistant to acylation. A solution of 12β-hydroxy compound (Ⅶ) in equal volumes of pyridine and Ac_2O was heated on boiling water bath for 16 hr., but the yield of diacetate were ca. 50% and less. White needles from MeOH, m.p. 134~137°, identical with an authentic sample prepared from pseudorockogenin diacetate. *Anal.* Calcd. for $C_{25}H_{36}O_5$: C, 72.08; H, 8.71. Found : C, 72.24; H, 8.93.

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Shigeru Sako*1 : Syntheses of Pyridazine Derivatives. Ⅳ.*2 Halogenopyridazine 1-Oxides.

(*National Institute of Hygienic Sciences*3)

In part Ⅱ[1] and Ⅲ*2 of this series, it was shown that the amino groups of 6-aminopyridazine 1-oxide and 4-amino-3,6-dimethylpyridazine 1-oxide were changed to chlorine by Gattermann reaction. The present paper describes the displacement of the amino groups on 3-, 4-, 5-, and 6-positions of pyridazine 1-oxide by diazotization and the preparation of several halogenopyridazine 1-oxides.

Oxidation of 5-amino-3,4-dichloropyridazine[2] (m.p. 178°) (Ⅰ) with an ethereal solution of monoperphthalic acid gave 77% of its N-oxide (Ⅱ). Ⅱ was also obtained by hydrogen peroxide-glacial acetic acid oxidation in a poor yield. Ⅱ was dehalogenated to 5-aminopyridazine N-oxide (Ⅲc) by catalitic hydrogenation over palladium-charcoal. Diazotization of Ⅲc in hydrochloric acid gave 5-chloropyridazine N-oxide (Ⅳ). The chlorine of Ⅳ was displaced to a methoxy group by sodium methoxide and this methoxy derivative was identical with 5-methoxypyridazine 1-oxide prepared by Natsume.[3] Thus, it became clear that Ⅱ, Ⅲc, and Ⅳ were 5-amino-3,4-dichloropyridazine 1-oxide, 5-aminopyridazine 1-oxide, and 5-chloropyridazine 1-oxide, respectively.

When 4-amino-3,5-dichloropyridazine[2] (m.p. 151°) (Ⅴ) was oxidized in ether with monoperphthalic acid, its N-oxide (Ⅵ) was obtained, in 43% yield. Treatment of Ⅵ in hydrochloric acid with sodium nitrite gave trichloropyridazine 1-oxide, which was identical with 3,4,5-trichloropyridazine 1-oxide (Ⅶ) prepared from Ⅱ by the same method. Accordingly, Ⅵ was 4-amino-3,5-dichloropyridazine 1-oxide.

3-, 4-, 5-, and 6-bromopyridazine 1-oxides (Ⅷa, Ⅷb, Ⅷc, and Ⅷd) were prepared by diazotization of corresponding aminopyridazine 1-oxides (Ⅲ) in hydrobromic acid, in 8%, 63% (Gattermann reaction), 40%, and 22% yield, respectively. 4-Bromopyridazine 1-oxide (Ⅷb) was easily prepared by heating 4-nitropyridazine 1-oxide[4] (Ⅸ) with hydrobromic acid.

*1 Present address : Ukima Plant, Chūgai Pharmaceutical Co., Ltd., Ukima, Kita-ku, Tokyo.

*2 Part Ⅲ. S. Sako : This Bulletin, **11**, 337 (1963).

*3 Tamagawa-yoga-machi, Setagaya-ku, Tokyo (佐子 茂).

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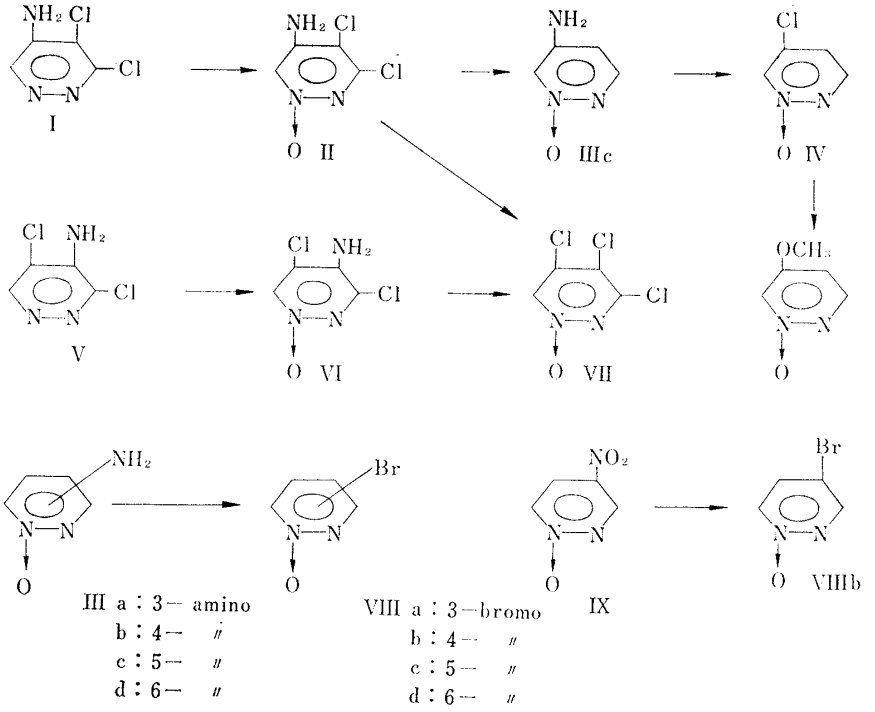

Chart 1.

The conclusion drawn from these experiments was as follows. N-oxidation of I and V gave their 1-oxides. The amino groups on 3-, 4-, 5-, and 6-positions of pyridazine 1-oxide were substituted with chlorine or bromine by diazotization though the yield of the 3-substituted derivative was poor. As there was no other suitable method, that of diazotization is usable for the preparation of 5- and 6-halogenopyridazine 1-oxide. II is important as the starting material for the preparation of 5-substituted pyridazine 1-oxides.

Experimental

5-Amino-3,4-dichloropyridazine 1-Oxide (II)——i) A mixture of 7.0 g. of I, 30 ml. of ether, 140 ml. of ethereal solution of monoperphthalic acid (containing 9.4 mg. of active 0 per ml., 1.9 mol. equiv.), and 10 ml. of MeOH was allowed to stand for 1 month in an ice box. The precipitate was filtered and washed with 50 ml. of MeOH. Pale orange crystals (5.9 g., 77%), m.p. 282°(decomp.), were recrystallized from MeOH to colorless prisms, m.p. 282°(decomp.). *Anal.* Calcd. for $C_4H_3ON_3Cl_2$: C, 26.69; H, 1.68; N, 23.35. Found : C, 26.87; H, 1.92; N, 23.32.

ii) A mixture of 220.1 mg. of I, 1.5 ml. of glacial AcOH and 0.25 ml. of 30% H_2O_2 was heated at 70° for 4 hr. After cooling, the precipitate was filtered, and 33.6 mg. (14%) of crystals, m.p. 230°(decomp.), were recrystallized from MeOH to colorless prisms, m.p. 282° (decomp.), which was found identical with II prepared above by mixed melting point and comparison of IR spectra.

4-Amino-3,5-dichloropyridazine 1-Oxide (VI)——A mixture of 900 mg. of V, 24 ml. of ethereal solution of monoperphthalic acid (containing 10.6 mg. of active 0 per ml., 2.9 mol. equiv.), and 3 ml. of MeOH was allowed to stand for 4 days at room temperature. The mixture was filtered, insoluble substance was added into a small amount of water, and neutralized with $NaHCO_3$. The precipitate was collected, and recrystallized from EtOH to slightly yellowish needles, m.p. 204°(decomp.), 422 mg. (43%). *Anal.* Calcd. for $C_4H_3ON_3Cl_2$: C, 26.69; H, 1.68; N, 23.35. Found : C, 27.13; H, 1.99; N, 22.54.

5-Aminopyridazine 1-Oxide (IIIc)——A mixture of 4.543 g. of II, 350 ml. of MeOH, and aqueous NaOH solution (2.8 g. of NaOH in 10 ml. of H_2O) was hydrogenated over Pd-C prepared from 15 ml. of 1% $PdCl_2$ and 0.7 g. of C. After 2 mol. equiv. of H_2 had been absorbed, the catalyst was filtered off, the filtrate was neutralized with HCl and evaporated under reduced pressure to dryness. The residue was extracted with 100 ml. of hot EtOH, the extract was concentrated to a small volume and allowed to stand at room temperature. The deposited crystals, m.p. 177~180°, were collected (2.341 g., 84%)

and recrystallized from EtOH to colorless prisms, m.p. 188.5~190°. *Anal.* Calcd. for $C_4H_5ON_3$: C, 43.24; H, 4.54; N, 37.83. Found: C, 43.16; H, 4.71; N, 37.92.

5-Chloropyridazine 1-Oxide (IV)——A mixture of 805.7 mg. of IIIc and 16 ml. of 27% HCl was heated into a solution and cooled. The amine hydrochloride was separated out as fine crystals. To this mixture, a solution of 635 mg. of $NaNO_2$ (1.3 mol. equiv.) in 4 ml. of H_2O was added, with shaking under ice cooling. After standing for 10 min. at room temperature, the reaction mixture was partially neutralized with $NaHCO_3$ and extracted with $CHCl_3$. The $CHCl_3$ layer was dried over anhyd. Na_2SO_4 and $CHCl_3$ was evaporated to dryness. An almost colorless crystalline product (367.7 mg.) was recrystallized from benzene to colorless needles, m.p. 115~117°, 289.3 mg. (31%). These needles were dissolved in benzene-$CHCl_3$, passed through a column of activated alumina, eluted with benzene-$CHCl_3$, and the solvent was evaporated from the eluate. A white crystalline product, m.p. 118.5~119.5°, was recrystallized from benzene to colorless needles, m.p. 119~120.5°. *Anal.* Calcd. for $C_4H_3ON_2Cl$: C, 36.80; H 2.32; N, 21.46. Found: C, 37.09; H, 2.21; N, 21.50.

Reaction of IV with Sodium Methoxide: Formation of 5-Methoxypyridazine 1-Oxide——A mixture of 40.2 mg. of IV, 0.8 ml. of MeOH and MeONa in MeOH (0.8 ml. containing 8 mg. of Na) was allowed to stand at 17° for 20 min. A small amount of water was added to the mixture. The solution was extracted with $CHCl_3$, the $CHCl_3$ layer was dried over anhyd. Na_2SO_4, and $CHCl_3$ was evaporated to dryness. A colorless crystalline product (26.2 mg., 67%), m.p. 106~109°, was recrystallized from benzene to colorless prisms, m.p. 109~111°, which were identical with the authentic sample of 5-methoxypyridazine 1-oxide[4] by mixed melting point and comparison of IR spectra.

3,4,5-Trichloropyridazine 1-Oxide (VII)——i) A mixture of 202.0 mg. of II, 4 ml. of 35% HCl, and 1 ml. of water was warmed until it went in solution and cooled. To this mixture, a solution of 112 mg. of $NaNO_2$ dissolved in 1 ml. of water was added under ice cooling. After standing for 5 min. at room temperature, the reaction mixture was partially neutralized with $NaHCO_3$ and extracted with $CHCl_3$. The $CHCl_3$ layer was dried over anhyd. Na_2SO_4, and $CHCl_3$ was evaporated to dryness. A brownish solid was recrystallized from petr. benzin to colorless scales, m.p. 124~125°, 82.3 mg. (37%). *Anal.* Calcd. for $C_4HON_2Cl_3$: C, 24.09; H, 0.51. Found: C, 24.07; H, 0.60.

ii) A mixture of 204.0 mg. of VI, 4 ml. of 35% HCl, and 1 ml. of water was treated as described above. Recrystallization from petr. benzin gave colorless needles, m.p. 124~125°, 81.6 mg. (36%). This was shown identical with VII, prepared above, by mixed melting point and comparison of IR spectra.

3-Bromopyridazine 1-Oxide (VIIIa)——To a solution of 274 mg. of 3-aminopyridazine 1-oxide[5] (IIIa) dissolved in 3 ml. of 47% HBr, 359 mg. (2.1 mol. equiv.) of $NaNO_2$ was added, under salt-ice cooling. The solution was partially neutralized and extracted with $CHCl_3$. The $CHCl_3$ layer was dried over anhyd. Na_2SO_4, and $CHCl_3$ was evaporated to dryness. The extract (386 mg.) was dissolved in benzene-$CHCl_3$, passed through a column of activated alumina, and eluted with benzene-$CHCl_3$. After evaporation of the solvent, the initial eluate left a brownish viscous substance, and 33.8 mg. (8%) of a white crystalline product, m.p. 117~121°, was obtained from the following eluate. The latter was recrystallized from benzene to colorless needles, m.p. 122~123°. *Anal.* Calcd. for $C_4H_3ON_2Br$: C, 27.45; H, 1.73; N, 16.01. Found: C, 27.76; H, 1.77; N, 16.38.

5-Bromopyridazine 1-Oxide (VIIIc)——A mixture of 110 mg. of IIIc, 1 ml. of 47% HBr, and 0.3 ml. of H_2O was treated with a solution of 120 mg. of $NaNO_2$ in 0.5 ml. of water, as described above for IV. The $CHCl_3$ extract was recrystallized from benzene to colorless needles, m.p. 117~119°, 70.1 mg. (40%). *Anal.* Calcd. for $C_4H_3ON_2Br$: C, 27.45; H, 1.73. Found: C, 27.58; H, 1.88.

6-Bromopyridazine 1-Oxide (VIIId)——A mixture of 525 mg. of 6-aminopyridazine 1-oxide (IIId) and 5 ml. of 47% HBr was treated with a solution of 670 g. of $NaNO_2$ in 2 ml. of water, as described above for IV. The residue from the $CHCl_3$ extract was recrystallized from benzene to colorless needles, m.p. 111~113°, 182.7 mg. (22%). *Anal.* Calcd. for $C_4H_3ON_2Br$: C, 27.45; H, 1.73. Found: C, 27.70; H, 1.90.

4-Bromopyridazine 1-Oxide (VIIIb)——i) A mixture of 1.011 g. of IX and 15 ml. of 47% HBr was heated on a steam bath for 4 hr. HBr was distilled off under reduced pressure, the residue was neutralized with $NaHCO_3$, extracted with $CHCl_3$, which was dried over anhyd. Na_2SO_4 and evaporated to dryness. The extract (1.041 g.), m.p. 95~100°, was dissolved in benzene-$CHCl_3$, passed through a column of activated alumina, eluted with benzene-$CHCl_3$. After evaporation of the solvent, 134 mg. of IX was recovered from the initial eluate. The crystalline product, m.p. 120~125°, obtained from the following eluate was recrystallized from benzene to colorless needles, m.p. 124~125.5°, 655 mg. (52%). *Anal.* Calcd. for $C_4H_3ON_2Br$: C, 27.45; H, 1.73; N, 16.01. Found: C, 27.75; H, 2.17; N, 16.26.

ii) To a solution of 107.6 mg. of 4-aminopyridazine 1-oxide[4] (IIIb) dissolved in 1 ml. of 24% HBr, a solution of 100 mg. of $NaNO_2$ in 0.5 ml. of water was added under ice cooling, followed by 20 mg. of Cu powder, and treated as described above. Yield, 105.9 mg. (63%).

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Summary

N-oxidation of 5-amino-3,4-dichloropyridazine and 4-amino-3,5-dichloropyridazine gave their 1-oxides. The amino groups on 3-, 4-, 5-, and 6-positions of pyridazine 1-oxide were substituted with chlorine or bromine by diazotization, but yield of 3-bromopyridazine 1-oxide was poor. 5-Amino-3,4-dichloropyridazine 1-oxide is usable as the starting material for the preparation of 5-substituted pyridazine 1-oxides.

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Masaichiro Masui and Hiroteru Sayo: Electron Spin Resonance of Free Radicals Electrochemically Generated from Polynitroalkanes.*1

(*Faculty of Pharmaceutical Sciences, Osaka University**2)

In the past several years, fairly many studies have been reported on the electron spin resonance (ESR) spectrum of aromatic nitro anion radicals,[1] but a few were reported on aliphatic nitro anion radicals,[2~6] especially on the radicals derived from aliphatic polynitro compounds only two papers being found. According to Adams, *et al.*[2] 2,2-dinitropropane gave no signal but tetranitromethane and dinitromethane gave well resolved spectra which were thought to be composed of several structures, but they did not give their hyperfine structures and isotropic coupling constants either. More recently, Lagercrantz[6] observed that a free radical produced by the reduction of tetranitromethane with sodium dithionite in alkaline aqueous solution showed an ESR spectrum of seven equally spaced lines (intensity ratio 1:3:6:7:6:3:1), from which they found the nitrogen coupling constant was 8.4 gauss and deduced that the radical was $[(NO_2)_3C\cdot]^{2-}$.

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*1 This paper is the Part XII of "Controlled Potential Electrolysis" (Part XI, M. Masui, H. Sayo, K. Kishi: Tetrahedron, **21**, 2831 (1965).

*2 Toneyama, Toyonaka-shi, Osaka-fu (桝井雅一郎, 佐用博照).

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