(B) For terpene alcohols: 1) conc. H_2SO_4–conc. H_3PO_4(1:9)
2) Ehrlich-Müller's reagent (alternative spraying of 5% AcOH solution of *p*-dimethylaminobenzaldehyde and conc. H_3PO_4)[4]
3) Fluorescein-bromine reagent[1]
4) Phosphomolybdic acid-conc. H_3PO_4(1:1)
(C) For carbonyl compounds: 1) 0.1% Solution of 2,4-dinitrophenylhydrazine reagent
2) Fluorescein-bromine reagent[1]
3) Ehrlich-Müller's reagent[4]

(Received September, 1, 1956)

3) F. Feigl, Y. Hashimoto: "Spot Tests," Elseviers Inc., Amsterdam, **II**, 226(1953).
4) H. Müller: Chem. Ztg., 673(1951).

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Tsukasa Kuraishi: 4,5-Substituted Pyridazines. I.

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In a previous paper,[1] the author reported the synthesis of 4-aminopyridazine and 4-amino-3,6-dichloropyridazine by heating 3,4,6-trichloropyridazine with dehyd. ethanolic ammonia solution. In order to carry out the synthesis of 4,5-substituted pyridazines, the reaction of mucochloric acid with hydrazine sulfate was attempted. Mowry[2] carried out the condensation of mucochloric acid with semicarbazide hydrochloride in the presence of potassium carbonate in 50% ethanol solution and heating in glacial acetic acid to give 4,5-dichloro-3-pyridazone. Mucobromic acid was condensed with hydrazine sulfate in aq. solution with use of sodium acetate by Grundmann.[3] These results have been extended to the preparation of similar 4,5-substituted pyridazines.

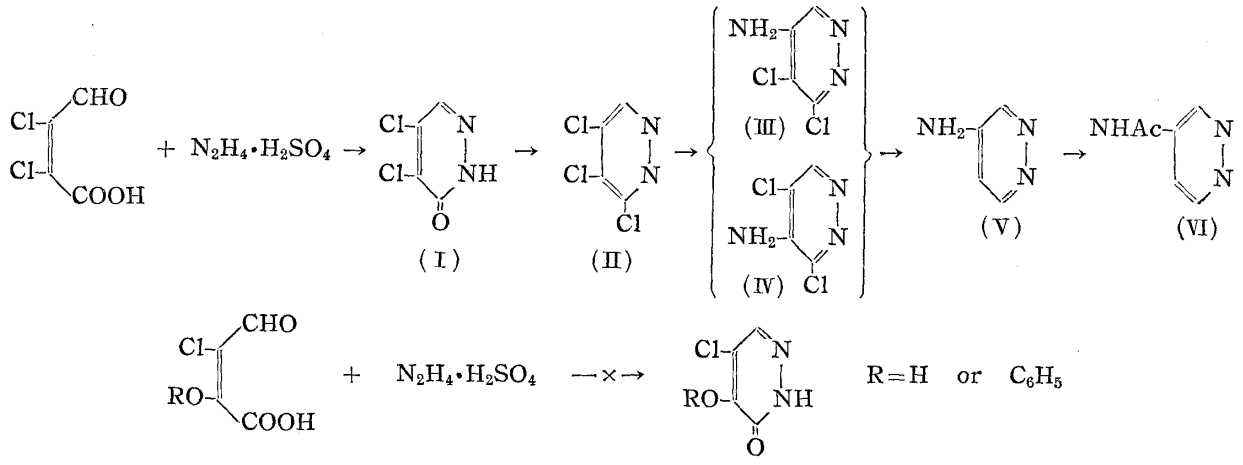
The present work was prompted by a desire to obtain 4,5-substituted pyridazines from 4,5-dichloropyridazone, which is obtained by the Grundmann's method, and derive them to 4-aminopyridazines.

Although the condensation of α-hydroxy- and -phenoxy-β-chloro-β-formylacylic acid (mucoxy- and mucophenoxy-chloric acid) were attempted, the desired products were not obtained by the Grundmann's method.

4,5-Dichloro-3-pyridazone was led to 3,4,5-trichloropyridazine by heating with phosphoryl chloride by the usual method. Replacement of chlorine in the trichloropyridazine with an amino group was attempted with a saturated ethanolic ammonia solution but only one chlorine was substituted even when heated at 130~140° for eight hours. 3-Amino-4,5-dichloropyridazine was not obtained but two isomers of another monoaminodichloropyridazine having m.p. 151°(III) and 178°(IV). These monoaminodichloropyridazines were derived to 4-aminopyridazines by catalytic reduction. The structures of the 4- or 5-aminodichloropyridazines (III and IV) are still in question.

Ultraviolet spectra of these aminodichloropyridazines in ethanol are given in Fig. 1. 4-Amino-3,6-dichloropyridazine shows the large shift of the weak bands at ca. 300 mμ to a longer wave length side from that of 4-aminopyridazine. The shift of the bands

* Schowa-machi, Nagasaki (倉石 典).
1) This Bulletin, **4**, 137(1956).
2) D. T. Mowry: J. Am. Chem. Soc., **75**, 1909(1953).
3) C. Grundmann: Ber., **81**, 1(1948).



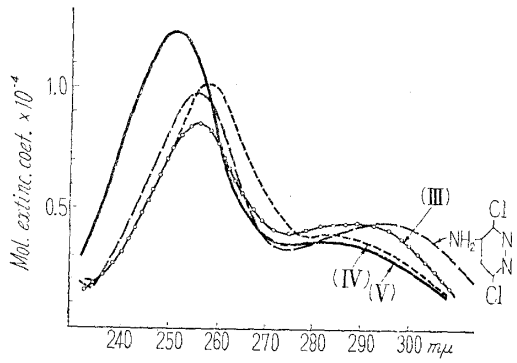


Fig. 1.
Urtraviolet Absorption Spectra of 4-Aminopyridazine and the Monoaminodichloropyridazine (in 95% EtOH)

in (III) and (IV) were found to be 5~6 mμ and 0~1 mμ, respectively. This may be due to the mutual configuration of the chlorine atoms bonded to the pyridazine ring, as mentioned earlier by Sklar.[4]

The author expresses his sincere thanks to Prof. M. Yanai for his encouragement and to Mr. T. Tachikawa for his technical assistance.

Experimental

(All m.p.s are uncorrected)

4, 5-Dichloro-3-pyridazone (I)—A mixture of 3.1 g. of hydrazine sulfate, 3 g. of AcONa was added to a conc. aq. solution of mucochloric acid (3.9 g.) at 80~100° with stirring. Separated crystals (3.5 g.) were filtered and recrystallized from water to prisms, m.p. 199~200°.[5] *Anal.* Calcd. for $C_4H_2ON_2Cl_2$: C, 29.09; H, 1.21. Found: C, 29.30; H, 1.26.

3, 4, 5-Trichloropyridazine (II)—Twenty grams of (I) was refluxed with 150 cc. of $POCl_3$ in an oil bath for 5 hrs. After removing the excess of $POCl_3$, the residue was poured into ice water and extracted with ether. 20 g. of a fraction of $b.p_{14\sim15}$ 117~118° was recrystallized from dil. acetone; m.p. 61°. *Anal.* Calcd. for $C_4HN_2Cl_3$: C, 26.15; H, 0.545. Found. C, 26.38; H, 0.61.

Aminodichloropyridazine (III and IV)—Eight grams of (II) was placed in a sealed tube with dehyd. EtOH saturated with NH_3 and heated in an oil bath at 120~130° for 5 hrs. After removal of the solvent, the residue was refluxed on a water bath with 20 cc. of $CHCl_3$ for 20 mins. and cooled at room temperature for several hours. The undissolved residue was separated and repeatedly recrystallized from water to 2.8 g. of (IV), prisms, m.p. 176~178°. *Anal.* Calcd. for $C_4H_3N_3Cl_2$: C, 29.25; H, 1.83. Found. C 29.16; H, 1.95.

The filtrate was evaporated and the residue was recrystallized from water giving thin needles (III), m.p. 150~151°; yield, 2 g.[6] *Anal.* Calcd. for $C_4H_3N_3Cl_2$: C, 29.25; H, 1.83. Found: C, 29.16; H, 1.95.

4) Sklar mentioned that the effect of molecular configuration on the spectra is the most sensitive in longest wave length band. cf. Rev. Mod. Phys., **14**, 233(1942).
5) D. T. Mowry (*loc. cit.*) recorded m.p. 202° for this compound.
6) Although the compound (IV) sometimes dissolved slightly in chloroform, it was isolated by recrystallization from water since it was less soluble in water than the compound (III).

4-Aminopyridazine (V)—i) A mixture of 2 g. of (III), 30 cc. EtOH, 0.98 g. NaOH, and 1.2 g. of 10% Pd-C was placed in a shaking flask and hydrogenated under atmospheric pressure. The solvent was removed on a water bath and the residue was completely dried and recrystallized from AcOEt; m.p. 128~129°. Yield, 0.5 g.

ii) A mixture of 2 g. of (IV), 5 cc. of conc. NH_3 (25%), 25 cc. of MeOH, and 1.4 g. of 8% Pd-C was treated as described above. After removing the solvent *in vacuo*, the residne was recrystallized from AcOEt; m.p. 125~127°. Yield, 0.4 g.

The samples showed no depression of m.p. with 4-amionpyridazine described in the preceding paper.[1]

4-Acetaminopyridazine (VI)—A mixture of 1 g. of (V) in 20 cc. of Ac_2O was refluxed very gently for 0.5 hr. and 1.1 g. of crude 4-acetaminopyridazine deposited from the solution on cooling was recrystallized from EtOH, m.p. 259~260°. *Anal.* Calcd. for $C_6H_7ON_3$: C, 52.55; H, 5.11. Found. C, 52.40; H, 4.54.

(Received September 6, 1956)