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Studies on Pyridazine 1,2-Dioxides. I. Syntheses of Pyridazine 1,2-Dioxides[1]

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When pyridazine (Ia), 3-methylpyridazine (IIa), 4-methylpyridazine (IIIa), 3,6-dimethylpyridazine (IVa) and their monoxides were oxidized with hydrogen peroxide in various conditions, the corresponding dioxides (Ib—IVb) were isolated. Although these dioxides were hardly react with PCl_3, the corresponding monoxides were obtained in catalytic reduction.

The results of ultraviolet, infrared and nuclear magnetic resonance spectrometries and polarographic reduction were described.

In the previous paper,[3] it has been reported that the oxidation of cinnoline with hydrogen peroxide in acetic acid gave cinnoline 1,2-dioxide and indazole in addition to the monoxides, and the structure of cinnoline 1,2-dioxide was confirmed by chemical and physico-chemical methods.

Although the preparation of cinnoline 1,2-dioxide,[3] 4-methylcinnoline 1,2-dioxide[4] and benzo(c)cinnoline 5,6-dioxide[5] were already reported, there have been no references concerning dioxide of pyridazine having adjacent nitrogens in monocyclic ring. The present paper deals with syntheses and properties of pyridazine 1,2-dioxide and its methyl derivatives.

When pyridazine (Ia), 3-methylpyridazine (IIa), 4-methylpyridazine (IIIa) and 3,6-dimethylpyridazine (IVa) were oxidized under various conditions as shown in Table VI and the products were chromatographed on an alumina column, the corresponding dioxides *i.e.*, pyridazine 1,2-dioxide (Ib), 3-methylpyridazine 1,2-dioxide (IIb), 4-methylpyridazine 1,2-dioxide (IIIb) and 3,6-dimethylpyridazine 1,2-dioxide (IVb) were isolated, besides their mono-N-oxides, in poor yields. By the same oxidation Ib and IVb could be obtained from pyridazine 1-oxide (Ic) and 3,6-dimethylpyridazine 1-oxide (IVc), respectively. Further, by the same conditions 3-methylpyridazine 1-oxide (IIc) and 3-methylpyridazine 2-oxide (IId) afforded IIb, and 4-methylpyridazine 1-oxide (IIIc) and 4-methylpyridazine 2-oxide (IIId) afforded IIIb, respectively.

The N-oxidation can be represented by Chart1.

Yields in method A, their physical properties and analytical data of these dioxides are tabulated in Table I.

In general, heterocyclic N-oxide group is deoxygenated by treatment of phosphorus trichloride in good yield. However, the dioxides of diazine having adjacent nitrogens, such as benzo(c)cinnoline 5,6-dioxide[5] and cinnoline 1,2-dioxide,[3] hardly react with phosphorus trichloride, and unchanged dioxides are recovered in 82% and 73% yields, respectively. When dioxides of pyridazine and methylpyridazines were refluxed with phosphorous trichloride

1) Preliminary report of this work was published in *Tetrahedron Letters*, **1968**, 1855.
2) Location: *18–1, Kamiyoga 1-chome, Setagaya-ku, Tokyo.*
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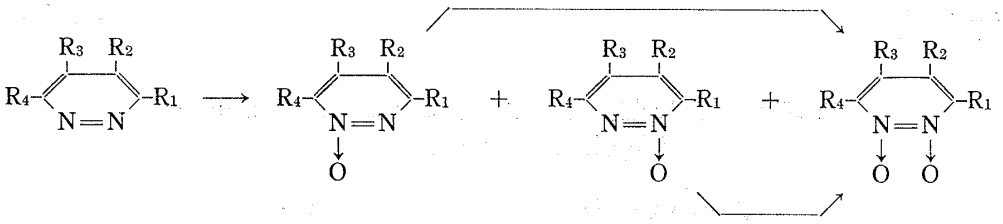

Ia: $R_1, R_2, R_3, R_4=H$ Ic: $R_1, R_2, R_3, R_4=H$ IId: $R_1=CH_3$, $R_2, R_3, R_4=H$ Ib: $R_1, R_2, R_3, R_4=H$
IIa: $R_1=CH_3$, $R_2, R_3, R_4=H$ IIc: $R_1=CH_3$, $R_2, R_3, R_4=H$ IIId: $R_2=CH_3$, $R_1, R_3, R_4=H$ IIb: $R_1=CH_3$, $R_2, R_3, R_4=H$
IIIa: $R_2=CH_3$, $R_1, R_3, R_4=H$ IIIc: $R_2=CH_3$, $R_1, R_3, R_4=H$ IIIb: $R_2=CH_3$, $R_1, R_3, R_4=H$
IVa: $R_1, R_4=CH_3$, $R_2, R_3=H$ IVc: $R_1, R_4=CH_3$, $R_2, R_3=H$ IVb: $R_1, R_4=CH_3$, $R_2, R_3=H$

Chart 1

TABLE I. Yields in Method A, Melting Points and Analytical Data of Pyridazine 1,2-Dioxides

Dioxide	Yield (%)	mp (°C)	Formula	Analysis (%)	
				Calcd.	Found
Pyridazine (Ib)	1.1 (from Ia) 1.0 (from Ic)	222 (decomp.)	$C_4H_4O_2N_2$	C: 42.86 H: 3.60 N: 24.99	43.11 3.74 25.28
3-Methylpyridazine (IIb)	1.2 (from IIa) 1.0 (from IIc) 0.8 (from IId)	156—157	$C_5H_6O_2N_2$	C: 47.62 H: 4.80 N: 22.22	47.40 4.88 22.46
4-Methylpyridazine (IIIb)	0.9 (from IIIa) 0.8 (from IIIc) 0.8 (from IIId)	150—150.5	$C_5H_6O_2N_2$	C: 47.62 H: 4.80 N: 22.22	47.77 4.85 22.03
3,6-Dimethylpyridazine (IVb)	9.7 (from IVa) 8.0 (from IVc)	216 (decomp.)	$C_6H_8O_2N_2$	C: 51.42 H: 5.75 N: 19.99	51.22 5.54 20.34

TABLE II. The Catalytic Reduction of Dioxides

Dioxides	Base	Products (%)		
		1-Oxide	2-Oxide	Recovery
Pyridazine (Ib)	—	60.7	—	—
3-Methylpyridazine (IIb)	—	—	87.2	3.5
4-Methylpyridazine (IIIb)	4.4	65.5	5.1	—
3,6-Dimethylpyridazine (IVb)	—	78.8	—	2.0
IVb[a)]	—	94.7	—	—
IVb[b)]	—	53.7	—	16.0

a) in basic solution *b*) in acidic solution

in chloroform, a trace of bases or monoxides is observed by thin-layer chromatography (TLC) and starting materials were recovered in 80—90% yields.

When the catalytic hydrogenation of dioxides over palladium charcoal in ethanol was stopped after uptake of about one mole of hydrogen, monoxides were isolated as major product, as shown in Table II.

The most interesting fact is that a large amount of IId and IIIc is formed in catalytic reduction of IIb and IIIb, in connection with the polarographic reduction to be described below.

The polarographic reduction of pyridazine dioxides was examined and the values of the half-wave potentials, $-E_{1/2}$, at two different pH are summarized in Table III.

Table III. Half-Wave Potentials, $-E_{1/2}$ (V), of Pyridazine N-Oxides

	pH 7.0	pH 10.0
Pyridazine	1.20	1.39
Pyridazine 1-oxide	1.40	1.51
Pyridazine dioxide	1.13, 1.40	1.14, 1.53
3-Methylpyridazine	1.19	1.41
3-Methylpyridazine 1-oxide	1.34	1.55
3-Methylpyridazine 2-oxide	1.47	1.58
3-Methylpyridazine dioxide	1.17, 1.47	1.19, 1.60
4-Methylpyridazine	1.23	1.44
4-Methylpyridazine 1-oxide	1.47	1.59
4-Methylpyridazine 2-oxide	1.43	1.57
4-Methylpyridazine dioxide	1.15, 1.47	1.20, 1.61
3,6-Dimethylpyridazine	1.00[a)]	1.34[a)]
3,6-Dimethylpyridazine 1-oxide	1.23[a)]	1.55[a)]
3,6-Dimethylpyridazine dioxide	1.23[a)]	1.21,[a)] 1.56[a)]

a) The half-wave potentials were measured against saturated calomel electrode at 30° and others were measured against Hg pool electrode at 25°.

Dioxides were reduced more easily than bases and monoxides, and appeared two reduction waves. The first half-wave potentials for dioxides may correspond to the reduction of dioxides to monoxides, and the half-wave potentials of second waves for dioxides nearly coincide with the half-wave potentials of monoxides. The similar trend has been also obtained from the reduction of dioxides of cinnoline,[3] benzo(c)cinnoline[5,6] and phenazine.[6] In view of above facts, dioxides were reduced first to monoxides (probably Ic, IId, IIIc and IVc) and then reduced to bases. The difference of reduction process in IIb and IIIb suggests that electron densities of nitrogens may be affected by methyl group.

As shown in Table IV, the ultraviolet (UV) spectra of these dioxides showed blue shift on increasing polarity of solvents.[7] However, the absorption maxima of dioxides in different concentrations of hydrochloric acid do not shift, and the spectra show only a slight hypochromic effect. On the other hand, UV spectra of pyridazine monoxides in different concentrations of hydrochloric acid show a characteristic blue shift accompanied with hypochromic effect. This property is compared in Fig. 1 for 3,6-dimethylpyridazine 1-oxide and the corresponding dioxide. In addition, these dioxides were produced no salts, like hydrochloride, picrate and perchlorate, and did not react boron trifluoride. It can be considered that these dioxides are less basic than the corresponding monoxides.

Infrared spectra of these dioxides showed no bands due to hydroxy and carbonyl groups. In cinnoline 1,2-dioxide[3] and 4-methylcinnoline 1,2-dioxide,[4] two bands at 1403 and 1343 cm^{-1}, and 1399 and 1342 cm^{-1} were assigned to the N–O stretching vibrations of dioxide group, respectively. Pyridazine dioxides exhibit two kinds of characteristic bands at around 1300—1380 cm^{-1} which may be assignable to the N–O stretching vibrations of dioxide group.

The 100 MHz nuclear magnetic resonance (NMR) spectra of these dioxides are shown in Fig. 2. Chemical shifts and spin spin coupling constants for individual protons of pyridazine

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Table V. UV and IR Spectral Properties of Pyridazine 1,2-Dioxides

Dioxide	Solvent	λmax, mμ (log ε)		ν_{N-O} $CHCl_3$ sol.		ν_{N-O} KBr disk	
Ib	dioxane	247 (4.43)	305 (3.91)	1380	1328	1350	1320
	EtOH	244 (4.44)	297 (3.84)				
	H_2O	241 (4.45)	288 (3.81)				
IIb	dioxane	248 (4.37)	305 (3.83)	1375	1310	1360	1300
	EtOH	244 (4.47)	296 (3.84)				
	H_2O	241 (4.46)	287 (3.87)				
IIIb	dioxane	249 (4.45)	305 (3.89)	1370	1308	1365	1305
	EtOH	246 (4.52)	296 (3.89)				
	H_2O	244 (4.54)	287 (3.92)				
IVb	dioxane	247 (4.43)	304 (3.85)	1372	1315	1364	1312
	EtOH	243 (4.48)	295 (3.86)				
	H_2O	239 (4.48)	286 (3.84)				

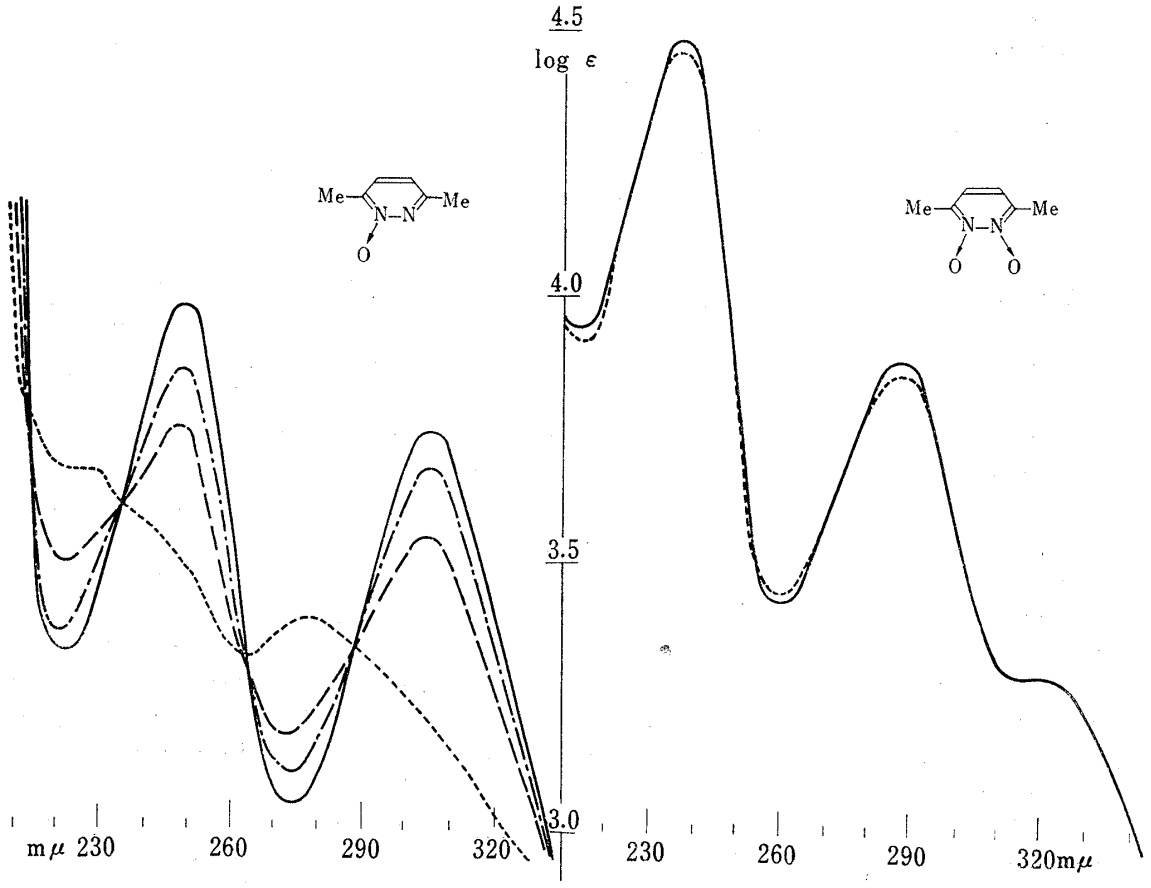

Fig. 1. Ultraviolet Absorption Spectra in Different Concentrations of Hydrochloric Acid

———: H_2O or 1N NaOH, —•—•—: 1N HCl, – – – –: 3N HCl, ·····: 5N HCl

1,2-dioxides are summarized in Table V. The spectrum of Ib consists of two symmetrical quartets of A_2X_2 type.[8,9] The spectrum of IVb shows two singlet peaks at 3.04 τ and 7.47 τ

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9) K. Tori and M. Ogata, *Chem. Pharm. Bull.* (Tokyo), **12**, 272 (1964).

Table V. 100 MHz NMR Spectral Parameters for Pyridazine 1,2-Dioxides

Dioxide	τ_3	τ_4	τ_5	τ_6	τ_{CH_3}	$J_{3,4}$	$J_{3,5}$	$J_{3,6}$	$J_{4,5}$	$J_{4,6}$	$J_{5,6}$
Ib	1.85	2.92	2.92	1.85	—	—	—	—	—	—	—
IIb	—	2.90	2.95	1.86	7.44	~0.4[a]	—	~0.6[a]	8.1	2.4	6.1
IIIb	1.93	—	3.02	1.89	7.65	~0.8[a]	2.4	0.7	~0.7[a]	—	6.8
IVb	—	3.04	3.04	—	7.47	<0.2[a]	—	—	—	—	<0.2[a]

chemical shift (τ), coupling constant, J(Hz) a) CH_3–H coupling

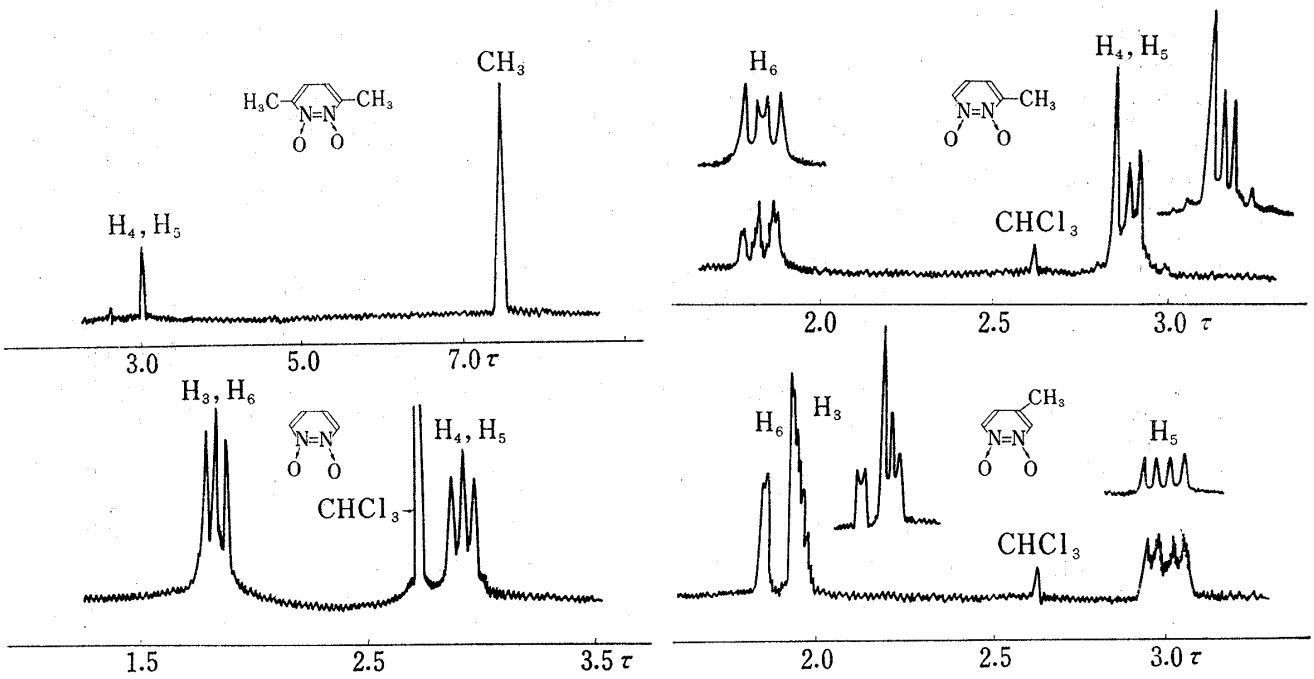

Fig. 2. NMR Spectra of Pyridazine 1,2-Dioxides at 100 MHz in $CDCl_3$

due to nuclear protons and methyl protons, respectively. The spectra of IIb and IIIb shown in Fig. 2 were analyzed from the irradiation of methyl protons. The observed NMR spectra of these dioxides are interpreted as di-N-oxide structure by comparing with the spectra of the parent bases and those of monoxides which have been interpreted by Tori, *et al.*[8,9] The complete assignment of dioxides will be reported elsewhere in future.

Further studies on pyridazine 1,2-dioxides are now in progress in our laboratory and will be reported in the following paper.

Experimental

Melting points were uncorrected. IR and UV spectra were measured on a JASCO model IR-S infrared spectrophotometer, and on a Hitachi model EPS-2 ultraviolet spectrophotometer. NMR spectra were determined at 100 MHz in $CDCl_3$ solutions containing tetramethylsilane as an internal standard using a Varian Model HA-100 Analytical NMR Spectrometer. Thin-layer chromatography was carried out on Merck's Aluminiumoxid G with the solvent systems of acetone–ethylacetate (1:19) and of benzene–acetone–ethanol (10:1:1).

Polarography——A Yanagimoto polarograph PA-101 with polarographic recoder was used. Half-wave potentials were measured with respect to the mercury pool electrode. The polarographic cell used was an H-type cell and general procedure was conventional. Reductions were measured at $25 \pm 1°$ in nitrogen with *ca.* 10^{-4} mole water–ethanol solutions in buffer solutions of pH 7.0 (McIlvaine buffer solution) and pH 10.0 (Sörensen buffer solution). The pH of these buffer solutions were checked with a glass electrode. Half-

wave potentials, $-E_{1/2}$, were estimated graphically. The values recorded in Table III are the means of three to five determinations. Diffusion currents were not measured.

Pyridazine 1,2-Dioxides (Ib—IVb)——Method A: A mixture of 1.2 g of 3,6-dimethylpyridazine (IVa), 30 ml of AcOH and 2 ml of 50% H_2O_2 was refluxed for 4 hr. To the mixture, 2 ml of 50% H_2O_2 was again added and refluxed for 5—8 hr, and further this procedure was repeated twice. To the reaction mixture a suitable quantity of H_2O was added, AcOH was evaporated under reduced pressure, and this procedure was repeated several times. The solution was basified with Na_2CO_3 and extracted with $CHCl_3$. The $CHCl_3$ layer was dried over anhyd. Na_2SO_4 and evaporated. The residue was dissolved in benzene–$CHCl_3$ and chromatographed on alumina. From the first fraction eluted with benzene, 3,6-dimethylpyridazine 1-oxide (IVc) was obtained. Yield, 512 mg (37.1%). The second fraction eluted with $CHCl_3$ gave white crystals. Recrystallization from acetone–EtOH gave 151 mg (9.7%) of 3,6-dimethylpyridazine 1,2-dioxide (IVb). Ib can be prepared from Ia and Ic by method A. IIa, IIc and IId afforded IIb and IIIa, IIIc and IIId afforded IIIb, respectively. IVb also can be prepared from IVc.

Method B: A mixture of 5.0g of IVa, 30ml of trifluoroacetic acid and 11 ml of 90% H_2O_2 preparing under cooling carefully was refluxed for 39 hr on a water bath, further 5 ml of 90% H_2O_2 was added, and the mixture again heated at the same temperature for 28 hr. Trifluoroacetic acid was evaporated under reduced pressure. The residue was diluted with a small quantity of H_2O, and then basified with Na_2CO_3 and extracted with $CHCl_3$. The $CHCl_3$ layer was dried over anhyd. Na_2SO_4 and evaporated. The residue was treated as described in method A. From the first fraction eluted with benzene, IVc was obtained. Yield, 1.08 g (18.8%). The second fraction eluted with $CHCl_3$ gave 1.07 g (16.5%) of IVb. IIIb can be prepared from IIIa with the same method.

Method C: To a suspended solution of 500 g of maleic anhydride and 500 ml of $CHCl_3$, 50 g of 90 % H_2O_2 was added with stirring in an ice bath. After stirring at the same temperature for 2 hr, 50 g of 3,6-dimethylpyridazine was added with small portions and continued stirring at room temperature for 7 days. A precipitates of maleic acid was filtered and washed with $CHCl_3$. The filtrate and washings were combined and washed with aqueous sodium carbonate solution. The $CHCl_3$ layer was dried over anhyd. Na_2SO_4 and evaporated. The residue was treated with the same way as described in Method A. 26.6 g (46.3%) of IVc and 8.7 g (13.4%) of IVb were obtained.

Method D: A mixture of 3.0 g of IVc, 100 mg of $Na_2WO_4 \cdot 2H_2O$ and 10 g of 50% H_2O_2 was warmed at 80° for 16 hr. After cooling, the mixture was extracted with $CHCl_3$, the $CHCl_3$ layer was dried over anhyd. Na_2SO_4 and evaporated. The residue was chromatographed on alumina. From benzene fraction IVc was recovered, 2.59 g (86.1%). The $CHCl_3$ fraction gave IVb, 166 mg (4.1%).

Method E: To a solution of 1.7 g of *m*-chloroperbenzoic acid (tech., 85%) in $CHCl_3$ IVc was added with stirring in an ice bath. After stirring at room temperature for 3 hr, 0.6 g of *m*-chloroperbenzoic acid was

Table VI. The Oxidation of Pyridazine and Methylpyridazines with H_2O_2 in Various Conditions

Material (g)	Method	Reaction		Yield (%)		
		Temperature	Time (hr)	Recovery	Monoxide	Dioxide
Ia (4.0)	A	refl.	43	—	58.4	1.1
Ic (1.8)	A	refl.	31	60.8	—	1.0
IIa (30.0)	A	refl.	42	—	73.8[a]	1.2
IIc (1.0)	A	refl.	46	13.2	—	1.0
IId (1.0)	A	refl.	49	36.8	—	0.8
IId (2.9)	A′	refl.	36	36.1	—	2.0
IIIa (2.0)	A	refl.	25	—	51.7[a]	0.9
IIIa (10.1)	B	refl.	56	—	27.2[a]	2.7
IIIc (1.0)	A	refl.	40	18.7	—	0.8
IIId (1.0)	A	refl.	45	19.1	—	0.8
IVa (1.2)	A	refl.	28	—	37.1	9.7
IVa (5.0)	A′	80—85°	67	—	46.0	11.8
IVa (5.0)	B	refl.	67	—	18.8	16.5
IVa (50.0)	C	25—30°	7days	—	46.3	13.4
IVc (5.0)	A	refl.	55	20.0	—	8.0
IVc (3.0)	D	80°	16	86.1	—	4.1
IVc (1.0)	E	refl.	27	62.0	—	1.5

A: AcOH+50% H_2O_2 A′: AcOH+90% H_2O_2 B: CF_3COOH+90% H_2O_2
C: maleic anhydride+90% H_2O_2 D: $Na_2WO_4 \cdot 2H_2O$+50% H_2O_2 E: 85% *m*-chlorobenzoic peracid in $CHCl_3$.
a) mixture of 1-oxide and 2-oxide

added, and the mixture was refluxed for 27 hr. After cooling, 10% sodium sulfite was added until iodide-starch test paper being negative. The mixture was extracted with $CHCl_3$, and $CHCl_3$ layer was washed with 5% $NaHCO_3$ solution and H_2O, and dried over anhyd. Na_2SO_4 and evaporated. The residue was treated with the same way as described A. 620 mg (62%) of IVc was recovered and 15 mg (1.5%) of IVb was obtained.

These results are summarized in Table VI.

Reactions of Pyridazine 1,2-Dioxides with PCl_3——To a solution of pyridazine 1,2-dioxides (Ib—IVb) (5—6×10^{-4} mole) in 2 ml of $CHCl_3$, a mixture of 0.4—0.5 g of PCl_3 in 1 ml of $CHCl_3$ was added and the mixture was refluxed for 4 hr. After cooling, the mixture was poured on crushed ice and basified with Na_2CO_3 and then extracted with $CHCl_3$. The $CHCl_3$ layer was dried over anhyd. Na_2SO_4 and evaporated. The residue was dissolved in benzene–$CHCl_3$ and chromatographed on alumina. The first fraction eluted with benzene showed a trace of corresponding bases and monoxides with TLC. From the second fraction eluted with $CHCl_3$ unchanged dioxides were recovered. These results are summarized in Table VII.

Table VII. Deoxygenation of Pyridazine Dioxides with PCl_3

Dioxide (mg)	PCl_3 (g)	Solvent	Reaction		Product[a]	Recovery (%)
			Temperature	Time (hr)		
Ib (70)	0.5	$CHCl_3$	refl.	4	Ia	66.6
IIb (60)	0.4	$CHCl_3$	refl.	4	IIa	72.3
IIIb (65)	0.45	$CHCl_3$	refl.	4	IIIa	30.8
IVb (150)	0.6	$CHCl_3$	refl.	6	none	87.3
IVb (100)	1.0	$CHCl_3$	refl.	10	IVc	48.0
IVb (100)	1.0	$CHCl_3$	refl.	36	IVc	26.3
IVb (100)	1.0	none	refl.	0.5	IVc	38.2

a) These were observed by TLC on alumina.

Catalytic Hydrogenation of Pyridazine 1,2-Dioxide (Ib)——A solution of 100 mg of Ib and Pd–C prepared from 2 ml of 1% $PdCl_2$ solution and 0.1 g of charcoal in 30 ml of EtOH was shaken in H_2 stream. After absorption of 1.1 moles of H_2, the catalyst was removed and the solvent was evaporated. The residue was dissolved in benzene and chromatographed on alumina. The first fraction eluted with benzene gave a trace of Ia with identical *Rf* value of its standard sample. From the second fraction eluted with the same solvent, 52 mg (60.7%) of colorless crystals were obtained, which was identified by TLC and IR spectrum comparison with authentic sample (Ic).

Catalytic Hydrogenation of 3-Methylpyridazine 1,2-Dioxide (IIb)——A solution of 100 mg of IIb and Pd–C prepared from 2 ml of 1% $PdCl_2$ solution and 0.1 g of charcoal in 30 ml of EtOH was shaken in H_2 stream. After absorption of 1.1 moles of H_2, the mixture was treated as described in catalytic hydrogenation of Ib. From the first fraction eluted with hexane–benzene, 3-methylpyridazine 2-oxide (IId) was obtained, which was identical by TLC and IR spectra of an authentic sample. Yield, 76.1 mg (87.2%). The second fraction eluted with $CHCl_3$ was recovered 3.5 mg (3.5%) of IIb.

Catalytic Hydrogenation of 4-Methylpyridazine 1,2-Dioxide (IIIb)——A solution of 100 mg of IIIb and Pd–C prepared from 2 ml of 1% $PdCl_2$ solution and 0.1 g of charcoal in 30 ml of EtOH was shaken in H_2 stream. The reduction was stopped after absorption of 1.1 moles of H_2 and the mixture was treated as described in Ib. From the first and second fractions eluted with benzene 3.3 mg (4.4%) of IIIa and 4.2 mg (5.1%) of IIId were recognized with TLC. The third fraction eluted with $CHCl_3$ gave 54.2 mg (65.5%) of IIIc, which was identical by IR spectrum and TLC of an authentic sample.

Catalytic Hydrogenation of 3,6-Dimethylpyridazine 1,2-Dioxide (IVb)——i) In Neutral Solution: A solution of 100 mg of IVb and Pd–C prepared from 2 ml of 1% $PdCl_2$ solution and 0.1 g of charcoal in 30 ml of EtOH was shaken in H_2 stream. After absorption of 1.0 mole of H_2, the mixture was treated as described in Ib. The first fraction eluted from benzene gave 70.1 mg (78.8%) of colorless needles, mp 110—111°. On admixture of this compound with authentic IVc showed no depression of the melting point and IR spectra of these compounds were identical. From the second fraction eluted from $CHCl_3$, 2.0 mg (2.0%) of IVb was recovered.

ii) In Basic Solution: A solution of 100 mg of IVb and Pd–C prepared from 2 ml of 1% $PdCl_2$ solution and 0.1 g of charcoal in 30 ml of EtOH containing 0.5 ml of 28% NH_4OH solution was treated as described in i). The fraction eluted from benzene gave 83.9 mg (94.7%) of IVc, mp 111—112°, which identified with the sample obtained in i).

iii) In Acidic Solution: A solution of 100 mg of IVb and Pd–C prepared from 2 ml of 1% $PdCl_2$ solution and 0.1 g of charcoal in 30 ml of EtOH containing 1 ml of 10% HCl solution was shaken in H_2 stream. After absorption of 1.3 moles of H_2, the catalyst was removed and solvent was evaporated. To the residue, a small amount of H_2O was added, basified with Na_2CO_3 and extracted with $CHCl_3$. The $CHCl_3$ layer was dried over anhyd. Na_2SO_4 and evaporated. The residue was dissolved in benzene and chromatographed on alumina. The first fraction eluted with benzene gave 47.6 mg (53.7%) of crystals which was identified with IVc. The second fraction eluted with the same solvent gave 3.2 mg of a mixture of IVc and IVb. From the third fraction eluted with $CHCl_3$, 16.0 mg (16.0%) of IVb was recovered.

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