[Chem. Pharm. Bull. 18(7)1340—1346(1970)]

UDC 547.852.3.04 : 541.45.04

Studies on Pyridazines. XV.[1] N-Oxidation of 3,3'-Bipyridazines and Reactions of Their N-Oxides

Hiroshi Igeta, Takashi Tsuchiya, Chisato Okuda and Hideharu Yokogawa

School of Pharmaceutical Sciences, Showa University[2]

(Received January 14, 1970)

N-Oxidation of 3,3'-bipyridazines (I, X, XXV) was carried out to form the corresponding N-oxides (II, III, XI, and XII). Reaction of the bipyridazines (I, X, and XX) with $POCl_3$–PCl_5 afforded the corresponding trichloromethyl compounds (VIII, and XXV) from I and XX, and the polychloro compounds (XVIII, and XIX), in which the chlorine atoms were substituted in the rings, from X. Treatment of the bipyridazine N-oxides (II, III, and XXI) with $POCl_3$, which have methyl groups α or γ-positions to the N-oxide groups, gave the corresponding chloromethyl compounds (VI, VII, and XXIII). And the reaction of the bipyridazine N-oxides (II and V) with Ac_2O afforded the corresponding acetoxy compounds (IV and III). In conclusion, the pattern of reactions of the 3,3'-bipyridazines and their N-oxides seems to be approximately analogous to that of monomeric pyridazines and their N-oxides.

In the preceding paper,[1] we have reported the syntheses of 3,3'-bipyridazines. In this paper we wish to describe some reactions of the bipyridazines.

Since pyridazine has vicinal two nitrogen atoms in the ring as hetero atoms, there is possibility of the formation of two kinds of isomeric mono-oxide in the N-oxidation of the unsymmetrically substituted pyridazines, on which many reports[3] have already been published, along with the reactivity of the N-oxides.

N-Oxidation of 3,3-bipyridazines was carried out to afford the corresponding N-oxides and several reactions, known in the monomeric pyridazine N-oxides, were applied to the dimeric N-oxides.

On the basis of the results obtained, some findings and the elucidation of the positions of the N-oxide groups were drawn out.

While 6,6'-dimethyl-3,3'-bipyridazine (I) was oxidized with H_2O_2 in acetic acid to afford the 1,1'-dioxide (II) in a good yield, the oxidation with equimolar perbenzoic acid gave the 1-mono-oxide (III) in 40% yield, accompanied by a small amount of the di-oxide (II). In both cases of the oxidation, the isomeric 2 (or 2')-oxide was not isolated.

Refluxing II and III with Ac_2O afforded 6,6'-di-acetoxymethyl-3,3'-bipyridazine (IV), and 6-mono-acetoxymethyl compound (V), respectively.

Reaction of II and III with $POCl_3$ gave 6,6'-bis-chloromethyl-3,3'-bipyridazine (VI), and 6-mono-chloromethyl compound (VII), respectively, in relatively good yields.

The nuclear magnetic resonance (NMR) spectra of the acetoxymethyl compounds (IV, V) and the chloromethyl compounds (VI, VII) exhibited singlet signals at around 5.4 δ for the former, and at around 4.9 δ for the latter due to the methylene groups, and also showed two sets of signals due to the ring protons, all of which are reasonable δ values to support the correctness of their structures.

The results are analogous to those obtained from the reaction of these reagents and monomeric pyridazine N-oxides[4] having methyl groups at α-position to the N-oxide groups.

1) Part XIV: H. Igeta, T. Tsuchiya, M. Nakajima, C. Okuda, and H. Yokogawa, *Chem. Pharm. Bull.* (Tokyo), **18**, 1228 (1970).
2) Location: *Hatanodai, Shinagawa-ku, Tokyo.*
3) E. Ochai, "Aromatic Amine Oxides," Elsevier, Amsterdam, 1967, and the references cited therein.
4) M. Kumagai, *J. Chem. Soc. Japan*, **81**, 350,1148 (1960); T. Nakagome, *Yakugaku Zasshi*, **82**, 249 (1962); M. Ogata, H. Kano, and K. Tori, *Chem. Pharm. Bull.* (Tokyo), **10**, 1123 (1962).

Accordingly, the oxygen atoms of II and III are apparently proved to be in the 1-positions. Moreover, II was identical with the compound obtained by the condensation reaction of 3-chloro-6-methyl-pyridazine 1-oxide.[1)]

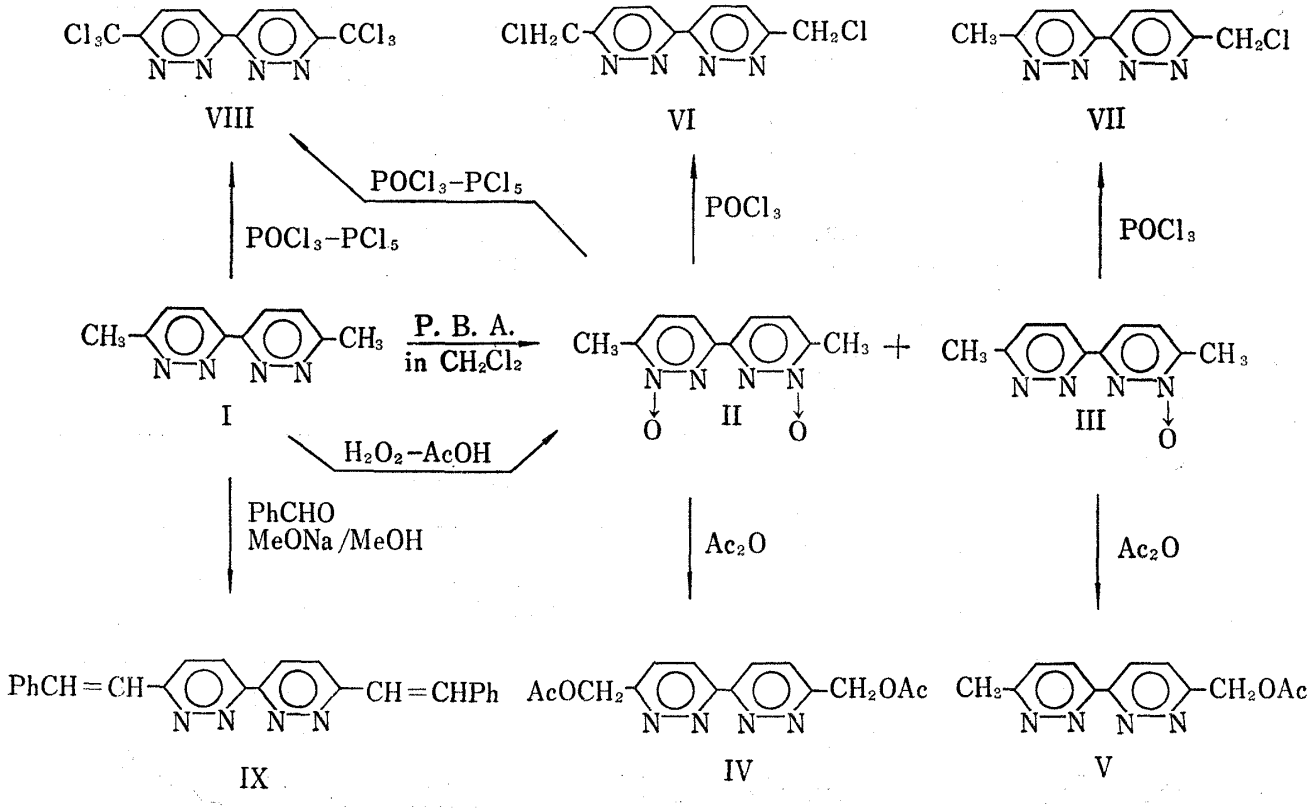

Chart 1

By heating I with a mixture of phosphoryl chloride and phosphorus pentachloride, 6,6′-bis-trichloromethyl-3,3′-bipyridazine (VIII) was obtained in 20% yield, which was also obtainable from the di-N-oxide (II) under similar condition.

The structural proof for VIII rests on the correct microanalytical result, molecular weight determination by mass spectrometry, and NMR spectra.

Chlorination of methyl group of monomeric pyridazine derivative with a mixture of phosphoryl chloride and phosphorus pentachloride has recently been noticed[5)] and similar observations have previously described on methylpyridines[6)] and methylpyrimidine N-oxides[7)] by Kato, *et al.*

As the characteristic reaction for reactive methyl group, the condensation reaction of I with benzaldehyde[8)] was carried out in the presence of CH_3ONa, affording 6,6′-distyryl-3,3′-bipyridazine (IX).

Oxidation of 6,6′-dimethoxy-3,3′-bipyridazine (X) with H_2O_2 in acetic acid afforded 2,2′-di-oxide (XI), and that with perbenzoic acid gave 2-mono-oxide (XII) and 2,2′-di-oxide (XI). No formation of the isomeric 1-oxide was observed in the both cases.

Refluxing these N-oxides with Ac_2O resulted in the recovery of the starting materials.

By reaction with $POCl_3$, the mono-oxide (XII) gave 5,6,6′-trichloro-3,3′-bipyridazine (XV), whereas the di-oxide (XI) afforded 5,5′, 6,6′-tetrachloro-3,3′-bipyridazine (XIV) in major and 5′-monochloro-6,6′-dimethoxy- 3,3′-bipyridazine 2-oxide (XIII) in minor.

5) C. Okuda, unpublished data.
6) T. Kato, H. Hayashi, and T. Anzai, *Yakugaku Zasshi*, **87**, 387 (1967).
7) T. Kato and H. Hayashi, *Yakugaku Zasshi*, **88**, 458 (1968).
8) T. Itai, S. Sako, and G. Okusa, *Chem. Pharm. Bull.* (Tokyo), **11**, 1146 (1963).

Table I. NMR Spectral Data[a)]

	δ				Miscellaneous[b)]
	H_4	$H_{4'}$	H_5	$H_{5'}$	
I	8.69	8.69	7.50	7.50	$-\underline{CH_3}$; 2.80
IV	8.61	8.61	7.94	7.94	$-\underline{CH}$–OAc; 5.39, –CO–$\underline{CH_3}$; 2.11_2
V	8.76	8.62	7.46	7.69	$-\underline{CH_3}$; 2.79, $-\underline{CH_2}$–OAc; 5.48, –CO–$\underline{CH_3}$; 2.19
VI	8.77	8.77	7.80	7.80	$-\underline{CH_2}Cl$; 4.91
VII	8.62	8.77	7.45	7.80[c)]	$-\underline{CH_3}$; 2.79, $-\underline{CH_2}Cl$; 4.91
VIII	8.97	8.97	8.60	8.60	
X	8.60	8.60	7.10	7.10	$-O\underline{CH_3}$; 4.19
XII	8.72	8.45	6.92	6.63	$-O\underline{CH_3}$; 4.15, $-O\underline{CH_{3'}}$; 4.03
VIII	8.46	8.90	6.73	—	$-O\underline{CH_3}$; 4.02, $-O\underline{CH_{3'}}$; 4.22
XIV	8.80	8.80	—	—	
XV	8.65	8.80	7.65	—	
XVI	8.64	8.64	7.94	7.94[c)]	
XVIII	—	—	7.70	7.70	
XIX	8.18	—	—	—	

	δ				Miscellaneous[b)]
	H_4	$H_{4'}$	H_6	$H_{6'}$	
XX	8.60	8.60	9.08	9.08	$-\underline{CH_3}$; 4.49
XXIII	8.71	8.71	9.23	9.23	$-\underline{CH_2}Cl$; 4.64
XXIV	8.56	8.56	—	—	$-\underline{CH_3}$; 2.51
XXV	9.75	9.75	9.23	9.23	

a) 60 M/C in $CDCl_3$ with TMS as internal reference *b*) $J_{4,5}$; 9.0—9.6 cps *c*) in DMSO-d_6

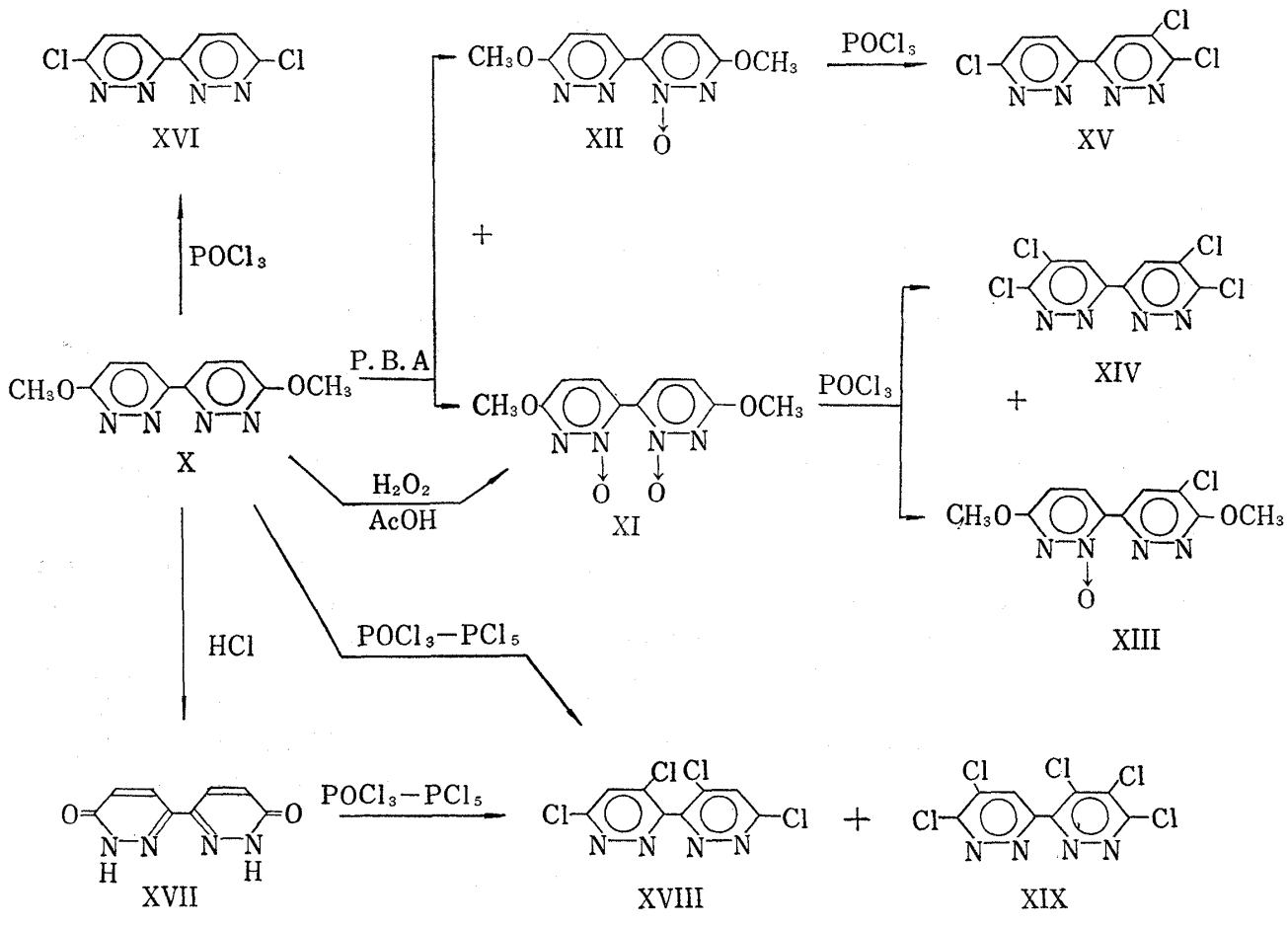

Chart 2

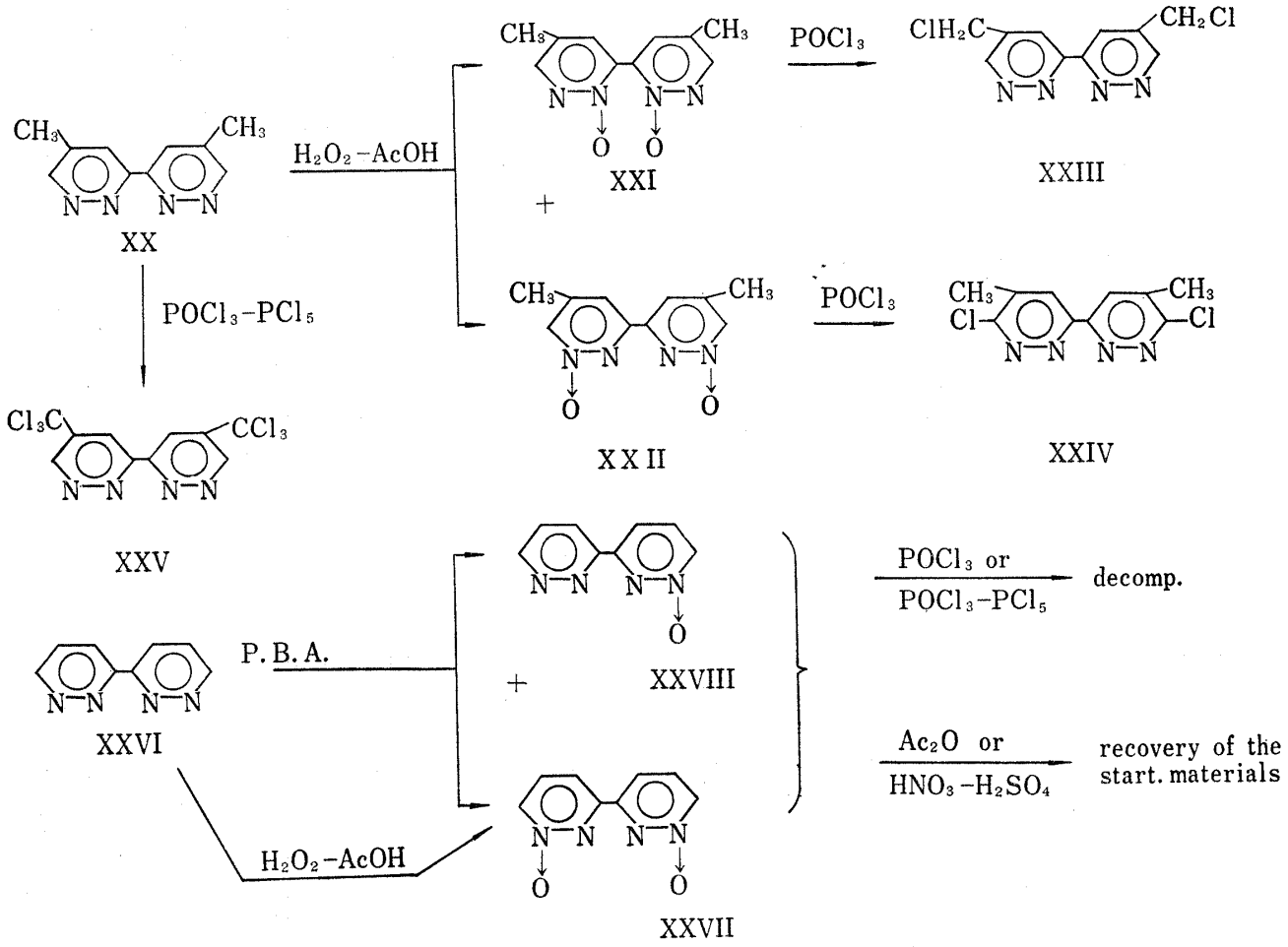

Chart 3

The formation of XIII suggests that chlorination at γ-position to the N-oxide group occurred at first and then replacement of methoxyl group with chlorine took place. On thin-layer chromatography (TLC), a couple of spots presumably due to the intermediates to XV and XIV developed, but their identifications could not be performed on account of small quantities.

Reaction of X with $POCl_3$ afforded 6,6′-dichloro-3,3′-bipyridazine (XVI) as a sole product, suggesting that in this reaction, the hydrogen atoms of the ring could not be replaced by chlorine atoms because of the absence of the polar effect of the N-oxide group.

From the results thus obtained, the oxygen atoms of the N-oxides (XI and XII) are proved to be in the 2-positions.

Reaction of X with $POCl_3$–PCl_5 afforded 4,4′,6,6′-tetrachloro-3,3′-bipyridazine (XVIII) and 4,5,5′,6,6′-pentachloro-3,3′-bipyridazine (XIX). XVIII was also obtained by reaction of $POCl_3$–PCl_5 and the bipyridazone (XVII), derived from X by hydrolysis with conc. HCl.

Each NMR spectrum of these polychloro compounds showed one singlet signal. Thus, the signal at 7.70 δ was assigned to $H_{5,5'}$ in the spectrum of XVIII, and 8.18 δ to H_4 in that of XIX.

The relatively higher field shift of these proton signals compared with those of other chloro compounds (Table I) might be due to the twist in the arrangement of two pyridazine rings by introduction of chlorine atom in the 4-position, and accordingly, to a decrease of the anisotropic influence of adjacent aromatic ring.[9]

9) O. Bastiansen, *Acta Chem. Scand.*, 4, 926 (1950).

Oxidation of 5,5′-dimethyl-3,3′-bipyridazine (XX) with H_2O_2 in acetic acid afforded two kinds of di-oxide, namely, 2,2′-dioxide (XXI) and 1,1′-dioxide (XXII) in 5% and 80% yields, respectively.

Reaction of these dioxides with $POCl_3$ afforded 5,5′-bis-chloromethyl-3,3′-bipyridazine (XXIII) from XXI and 6,6′-dichloro-5,5′-dimethyl-3,3′-bipyridazine (XXIV) from XXII, respectively.

Heating these bipyridazine di-oxides (XXI, XXII) with Ac_2O resulted in the recovery of the starting materials.

Reaction of XX with $POCl_3$–PCl_5 afforded 5,5′-bis-trichloromethyl-3,3′-bipyridazine (XXV), similar to the case of I.

In the oxidation of 3,3′-bipyridazine (XXVI), 1,1′-di-oxide (XXVII) was obtained by H_2O_2–AcOH, and 1-mono-oxide (XXVIII) and the di-oxide (XXVII) were obtained by perbenzoic acid, and the isomeric 2-oxides were not obtained in the both oxidation reactions. XXVII was identical with the sample synthesized by an alternative method described in the preceeding paper.[1)]

Reaction of these N-oxides with Ac_2O resulted in the recovery of the starting materials. Reaction of them with $POCl_3$ or $POCl_3$–PCl_5 afforded tarry substances and any definite compound was not isolated.

These experimental results have revealed that in the N-oxidation of 3,3′-bipyridazines, the nitrogen atoms adjacent to the carbon atom which bears an aromatic ring or a methoxyl group, could hardly be attacked.

These facts are well agreed with the observations noticed in monomeric pyridazines, namely, in the case of 3-phenyl- or 3-methoxy-pyridazine, N-oxidation of the 1-position predominates.[10,11)]

In conclusion, the pattern of the reactions of 3,3′-bipyridazines and their N-oxides seems to be approximately analogous to that of monomeric pyridazines and their N-oxides.

Experimental

N-Oxidation of I: Formation of 6,6′-Dimethyl-3,3′-bipyridazine 1,1′-Dioxide (II) and 6,6′-Dimethyl-3,3′-bipyridazine 1-Oxide (III)——i) With Hydrogen Peroxide: The bipyridazine (I) (5 g) was dissolved in acetic acid (40 ml) and 30% H_2O_2 (15 ml) was added. The solution was warmed at 70—80° for 3 hr and then another 10 ml of H_2O_2 was added and kept for further 3 hr at the same temperature. After cool, the separated crystals were collected by filtration. The filtrate was condensed to a small volume *in vacuo* and the separated crystals were again collected. Recrystallization of the crystals (4.8 g) from MeOH gave needles (II) (4.2 g), mp 293—294° (decomp.). *Anal.* Calcd. for $C_{10}H_{10}O_2N_4$: C, 55.04; H, 4.62; N, 25.68. Found: C, 55.44; H, 4.64; N, 25.47.

ii) With Perbenzoic Acid: The bipyridazine (I) (3 g) was dissolved in CH_2Cl_2 (50 ml) containing 1.2 equimolar perbenzoic acid, and the solution was kept in ice-box for 2 days. The separated crystaks were collected by filtration and washed with ether and then recrystallized from MeOH to needles (0.4 g), mp 293—294° (decomp.), undepressed on admixture with the 1,1′-dioxide (II).

The filtrate was washed with 5% NaOH and water, and then dried on Na_2SO_4. After removal of the solvent, the residue was dissolved in C_6H_6–CH_2Cl_2 (1:1) and passed through a column of alumina. From the eluate with C_6H_6–CH_2Cl_2, 0.9 g of the starting material was recovered. The column was again eluted with CH_2Cl_2 and the eluate was evaporated to dryness. The solid was recrystallized from AcOEt to crystals (III), mp 230°. *Anal.* Calcd. for $C_{10}H_{10}ON_4$: C, 59.39; H, 4.98; N, 27.71. Found: C, 59.39; H, 4.96; N, 27.72.

Reaction of II with $POCl_3$: Formation of 6,6′-Bis-chloromethyl-3,3′-bipyridazine (VI)——A mixture of II (1 g) and $POCl_3$ (8 ml) was heated on a boiling water bath for 4 hr. The excess $POCl_3$ was removed *in vacuo*, and the residue was poured onto ice. The mixture was neutrallized with $NaHCO_3$ and extracted with CH_2Cl_2. The extract was washed with water and dried on Na_2SO_4 and evaporated to dryness. The residue was dissolved in C_6H_6 and passed through a column of alumina to remove coloured material, and then C_6H_6 was evaporated from the eluate. The solid thus obtained was recrystallized from benzene to crystals (VI) (0.85 g), mp 199—200°. *Anal.* Calcd. for $C_{10}H_8N_4Cl_2$: C, 47.09; H, 3.16; N, 21.97. Found: C, 47.14; H, 3.11; N, 21.75.

10) M. Ogata, *Chem. Pharm. Bull.* (Tokyo), **11**, 1522 (1963).
11) H. Igeta, *Chem. Pharm. Bull.* (Tokyo), **7**, 293 (1959); T. Itai and S. Sako, *ibid.*, **10**, 989 (1962); M. Ogata and H. Kano, *ibid.*, **11**, 29 (1963); T. Horie and T. Ueda, *ibid.*, **11**, 114 (1963).

Reaction of II with Ac_2O: Formation of 6,6′-Bis-acetoxymethyl-3,3′-bipyridazine (IV)——A mixture of II (0.5 g) and Ac_2O (4 ml) was refluxed for 4 hr and the excess Ac_2O was removed *in vacuo*. The residue was dissolved in benzene and passed through a column of alumina and then eluted with AcOEt. The eluate was evaporated to dryness, and the solid thus obtained was recrystallized from benzene to crystals (IV) (0.45 g), mp 167—168°. *Anal.* Calcd. for $C_{14}H_{14}O_4N_4$: C, 55.62; H, 4.67; N, 18.54. Found: C, 55.32; H, 4.55; N, 18.40.

Reaction of III with Ac_2O: Formation of 6-Acetoxymethyl-3,3′-bipyridazine (V)——A mixture of III (0.1 g) and Ac_2O (3 ml) was refluxed for 4 hr and the excess Ac_2O was removed *in vacuo*. The residue was dissolved in benzene and passed through a column of alumina, and eluted with C_6H_6–CH_2Cl_2 (1:1). The eluate was evaporated to dryness and the solid was recrystallized from benzene to crystals (V) (0.065 g), mp 176°. *Anal.* Calcd. for $C_{12}H_{12}O_2N_4$: C, 58.06; H, 4.87; N, 22.94. Found: C, 58.36; H, 5.09; N, 22.60.

Reaction of III with $POCl_3$: Formation of 6-Chloromethyl-6′-methyl-3,3′-bipyridazine (VII)——A mixture of III (0.5 g) and $POCl_3$ (5 ml) was refluxed for 3 hr and the excess $POCl_3$ was removed *in vacuo*. The residue was poured onto ice, neutrallized with conc. NH_4OH, and then extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with water, dried on Na_2SO_4 and the solvent was evaporated. The residue was dissolved in benzene and passed through a column of alumina, and eluted with benzene. The eluate was evaporated and the solid was recrystallized from benzene to crystals (VII) (0.48 g), mp 173-175°. *Anal.* Calcd. for $C_{10}H_9N_4Cl$: C, 54.42; H, 4.08; N, 25.39. Found: C, 54.04; H, 4.28; N, 25.12.

Reaction of I with $POCl_3$-PCl_5: Formation of 6,6′-Bis-trichlomethyl-3,3′-bipyridazine (VIII)——A mixture of I (0.5 g), $POCl_3$ (10 ml) and PCl_5 (10 g) was heated at 150° for 3 hr. The reaction mixture was poured onto ice and neutrallized with conc. NH_4OH, and then extracted with CH_2Cl_2. The extract was washed with water and dried on Na_2SO_4. The solvent was evaporated and the residue was dissolved in benzene, passed through a column of alumina, and eluted with benzene. The eluate was evaporated and the solid was recrystallized from benzene to crystals (VIII) (0.25 g), mp over 300°. *Anal.* Calcd. for $C_{10}H_4N_4Cl_6$: C, 30.53; H, 1.02; N, 14.25. Found: C, 30.79; H, 1.03; N, 13.80.

6,6′-Distyryl-3,3′-bipyridazine (IX)—To a solution of I (0.2 g) and benzaldehyde (1 g) dissolved in MeOH (3 ml), MeONa (prepared from 0.2 g of Na and 3 ml of MeOH) was added and the whole was heated in a sealed tube at 100° for 5 hr. After cool, the separated crystals were collected and recrystallized from MeOH to crystals, mp over 300° (0.32 g). *Anal.* Calcd. for $C_{24}H_{18}N_4$: C, 79.53; H, 5.01; N, 15.46. Found: C, 79.77; H, 4.89; N, 15.50.

N-Oxidation of X: Formation of 6,6′-Dimethoxy-3,3′-bipyridazine 2,2′-Dioxide (XI) and 6,6′-Dimethoxy-3,3′-bipyridazine 2-Oxide (XII)——i) With Hydrogen Peroxide: According to the procedure described for II, X (5 g) was treated similarly and worked up. The solid thus obtained was recrystallized from MeOH–AcOEt to crystals (XI) (4.8 g), mp 258—259°. *Anal.* Calcd. for $C_{10}H_{10}O_4N_4$: C, 48.00; H, 4.02; N, 22.39. Found: C, 48.03; H, 4.06; N, 22.36.

ii) With Perbenzoic Acid: A mixture of X (3 g) and CH_2Cl_2 (50 ml) containing 1.2 equimolar perbenzoic acid, was allowed to stand for 2 days in ice-box. The separated crystals (XI) (1 g) were collected. The filtrate was washed with 5% NaOH and water, and then dried on Na_2SO_4. After removal of solvent, the residue was dissolved in benzene and passed through a column of alumina. From the benzene eluate, 0.7 g of the starting material (X) was recovered. Then, the column was eluted with C_6H_6–CH_2Cl_2 (1:1). The eluate was evaporated and the solid was recrystallized from MeOH to crystals (XII) (0.5 g), mp 195°. *Anal.* Calcd. for $C_{10}H_{10}O_3N_4$: C, 51.28; H, 4.30; N, 23.92. Found: C, 51.08; H, 4.30; N, 23.93.

Reaction of XI with $POCl_3$: Formation of 5,5′,6,6′-Tetrachloro-3,3′-bipyridazine (XIV) and 5′-Chloro-6,6′-dimethoxy-3,3′-bipyridazine 2-Oxide (XIII)——A mixture of XI (0.4 g) and $POCl_3$ (10 ml) was refluxed for 4 hr and the excess $POCl_3$ was removed *in vacuo*. The residue was poured onto ice, neutrallized with conc. NH_4OH, and then extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with water, dried on Na_2SO_4, and evaporated. The tarry residue was dissolved in benzene, passed through a column of alumina and eluted with benzene. The eluate was evaporated and the solid was recrystallized from benzene to prisms (XIV) (0.18 g), mp 238—240°. *Anal.* Calcd. for $C_8H_2N_4Cl_4$: C, 32.43; H, 0.78; N, 18.91. Found: C, 32.75; H, 0.67; N, 19.13.

After elution with benzene, the column was again eluted with CH_2Cl_2. The eluate was evaporated and the solid was recrystallized from AcOEt to crystals (XIII) (0.03 g), mp 220—221°. *Anal.* Calcd. for $C_{10}H_9O_3N_4Cl$: C, 44.76; H, 3.38; N, 20.87. Found: C, 44.70; H, 3.21; N, 20.63.

Reaction of XII with $POCl_3$: Formation of 5,6,6′-Trichloro-3,3′-bipyridazine (XV)——A mixture of XII (0.2 g) and $POCl_3$ (5 ml) was refluxed for 4 hr and worked up similarly to the procedure described for XI. The tarry residue thus obtained was dissolved in benzene and purified by column chromatography on alumina. The benzene eluate was evaporated and the solid was recrystallized from benzene to crystals (XV) (0.06 g), mp 172°. *Anal.* Calcd. for $C_8H_3N_4Cl_3$: C, 36.74; H, 1.16; N, 21.43. Found: C, 36.61; H, 1.08; N, 21.13.

Reaction of X with $POCl_3$: Formation of 6,6′-Dichloro-3,3′-bipyridazine (XVI)——A mixture of X (0.6 g) and $POCl_3$ (10 ml) was refluxed for 3 hr and worked up similarly to the procedure described for XI. The tarry residue was dissolved in benzene and purified by column chromatography on alumina. The benzene eluate was evaporated and the solid was recrystallized from benzene to crystals (XVI) (0.41 g), mp above 290° (decomp.). *Anal.* Calcd. for $C_8H_4N_4Cl_2$: C, 42.29; H, 1.76; N, 24.66. Found: C, 42.43; H, 1.75; N, 24.64.

Reaction of X with $POCl_3$-PCl_5: Formation of 4,4′,6,6′-Tetrachloro-3,3′-bipyridazine (XVIII)——A mixture of X (0.5 g), $POCl_3$ (5 ml) and PCl_5 (5 g) was heated at 130—150° over night. The reaction mixture was poured onto ice, neutrallized with conc. NH_4OH, and then extracted with CH_2Cl_2. The CH_2Cl_2 layer was treated as usual, and the tarry residue was dissolved in benzene and purified by column chromatography on alumina. The benzene eluate was evaporated and the solid was recrystallized from C_6H_6–ether to crystals (XVIII) (0.06 g), mp 170°. *Anal.* Calcd. for $C_8H_2N_4Cl_4$: C, 32.43; H, 0.67; N, 18.91. Found: C, 32.73; H, 0.80; N, 18.89.

3,3′-Bipyridazine-6,6′(1H,1′H)-dione (XVII)——To X (1 g), hydrochloric acid (5 ml) was added and the whole was heated on a boiling water bath for 6 hr. After cool, the separated white powder was collected by filtration and washed with water and then with hot MeOH. This was insoluble in most of solvent sand has mp above 300°. IR (KBr): 1625 cm^{-1} (amide) 2800 cm^{-1} (>NH). *Anal.* Calcd. for $C_8H_6O_2N_4$: C, 50.53; H, 3.18; N, 29.47. Found: C, 49.80; H, 3.10; N, 28.50.

Reaction of XVII with $POCl_3$-PCl_5: Formation of 4,5,5′,6,6′-Pentachloro-3,3′-bipyridazine (XIX) and 4,4′,6,6′-Tetrachloro-3,3′-bipyridazine (XVIII)——A mixture of XVII (0.3 g), $POCl_3$ (4.5 ml) and PCl_5 (7.5 g) was heated at 130—140° for 4 hr and treated similarly to the case of X. The tarry residue was dissolved in benzene and purified by column chromatography on alumina. The first fraction was evaporated and the solid was recrystallized from C_6H_6–ether to crystals (XIX) (0.04 g), mp 160—161°. *Anal.* Calcd. for $C_8HN_4Cl_5$: C, 29.09; H, 0.33; N, 16.97. Found: C, 29.21; H, 0.66; N, 16.72.

The second fraction was evaporated and the solid was recrystallized from C_6H_6–ether to crystals, mp 170°, undepressed on admixture with the sample (XVIII) obtained by reaction of X with $POCl_3$–PCl_5.

N-Oxidation of XX with H_2O_2: Formation of 5,5′-Dimethyl-3,3′-bipyridazine 1,1′-Dioxide (XXII) and 5,5′-Dimethyl-3,3′-bipyridazine 2,2′-Dioxide (XXI)——To a solution of XX (0.6 g)(dissolved) in acetic acid (6 ml), 30% H_2O_2 (3 ml) was added and the whole was warmed at 60—70° for 3 hr, and then additional H_2O_2 (3 ml) was added and the solution was kept at the same temperature for further 3 hr. After cool, the separated crystals were collected by filtration. Water was added to the filtrate, which was condensed to a small volume, and the separated crystals were again collected. The crystals were recrystallized from MeOH to crystals (XXII) (0.48 g), mp 276—279°.

The filtrate was then neutrallized with Na_2CO_3 and extracted with CH_2Cl_2. The CH_2Cl_2 layer was dried on Na_2SO_4, and evaporated. The residue was recrystallized from MeOH to crystals (XXI) (0.04 g), mp 251—253°. *Anal.* Calcd. for $C_{10}H_{10}O_2N_4$: C, 55.04; H, 4.62; N, 25.68. Found for XXII: C, 54.92; H, 4.42; N, 25.29. for XXI: C, 55.20; H, 4.53; N, 25.19.

Reaction of XXI with $POCl_3$: Formation of 5,5′-Bis-chloromethyl-3,3′-bipyridazine (XXIII)——A mixture of XXI (20 mg) and $POCl_3$ (2 ml) was refluxed for 3 hr and treated similarly to the case of the reaction of II and $POCl_3$. The resulted tarry substance was dissolved in benzene and purified by column chromatography on alumina. Evaporation of the benzene eluate afforded a syrup (XXIII) (*ca.* 5 mg). TLC, one spot; GLC, one peak. The structure was elucidated from the NMR spectrum (Table I).

Reaction of XXII with $POCl_3$: Formation of 5,5′-Dimethyl-6,6′-dichloro-3,3′-bipyridazine (XXIV)——A mixture of XXII (0.2 g) and $POCl_3$ (5 ml) was refluxed for 3 hr and worked up as usual. The residue was dissolved in benzene and purified by column chromatography on alumina. The benzene eluate was evaporated and the solid was recrystallized from benzene to crystals (XXIV) (0.11 g), mp 242°. *Anal.* Calcd. for $C_{10}H_8N_4Cl_2$: C, 47.06; H, 3.13; N, 21.83. Found: C, 47.25; H, 3.33; N, 21.96.

Reaction of XX with $POCl_3$-PCl_5: Formation of 5,5′-Bis-trichloromethyl-3,3′-bipyridazine (XXV)——A mixture of XX (0.3 g), $POCl_3$ (5 ml) and PCl_5 (5 g) was heated at 130—150° for 4 hr and worked up as usual. The residue was dissolved in benzene and purified by column chromatography on alumina. The benzene eluate was evaporated and the solid was recrystallized from benzene–*n*-hexane to crystals (XXV) (0.54 g), mp 227°. *Anal.* Calcd. for $C_{10}H_4N_4Cl_6$: C, 30.52; H, 1.02; N, 14.25. Found: C, 30.53; H, 1.12; N, 14.35.

N-Oxidation of XXVI: Formation of 3,3′-Bipyridazine 1,1′-Dioxide (XXVII) and 3,3′-Bipyridazine 1-Oxide (XVIII)——i) With Hydrogen Peroxide: To XXVI (3 g) dissolved in acetic acid (15 ml), 30% H_2O_2 (7 ml) was added and the solution was kept at 70—80° for 3 hr, and additional H_2O_2 (7 ml) was added. The solution was kept at the same temperature for further 3 hr. After cool, the separated crystals were collected. The filtrate was condensed to a small volume, to which some water was added, and the separated crystals were again collected. The crystals were recrystallized from aqueous MeOH to needles (XXVII) (3.1 g), mp 320°. *Anal.* Calcd. for $C_8H_6O_2N_4$: C, 50.53; H, 3.18; N, 29.47. Found: C, 50.14; H, 3.15; N, 29.08.

ii) With Perbenzoic Acid: A mixture of XXVI (3 g) and CH_2Cl_2 (40 ml) containing 1.2 equimolar perbenzoic acid was kept in ice box for 2 days. The separated crystals were collected and extracted with MeOH while hot. The residual crystal was recrystallized from aqueous MeOH to crystal (XXVII) (0.1 g). The MeOH extract was condensed to a small volume and the separated crystals was collected. The crystal was purified by repeated recrystallization from MeOH to crystal (XXVIII) (2.6 g), mp 269—271°. *Anal.* Calcd. for $C_8H_6ON_4$: C, 55.17; H, 3.47; N, 32.17. Found: C, 54.67; H, 3.47; N, 31.90.

Acknowledgement The authors wish to express their deep appreciation to Mrs. Y. Ishiguro and Miss T. Kihara for elemental microanalyses, to Miss F. Suzuki for measurements of NMR spectra.