New Derivatives of Pyridazino[4,5-*d*]pyridazine

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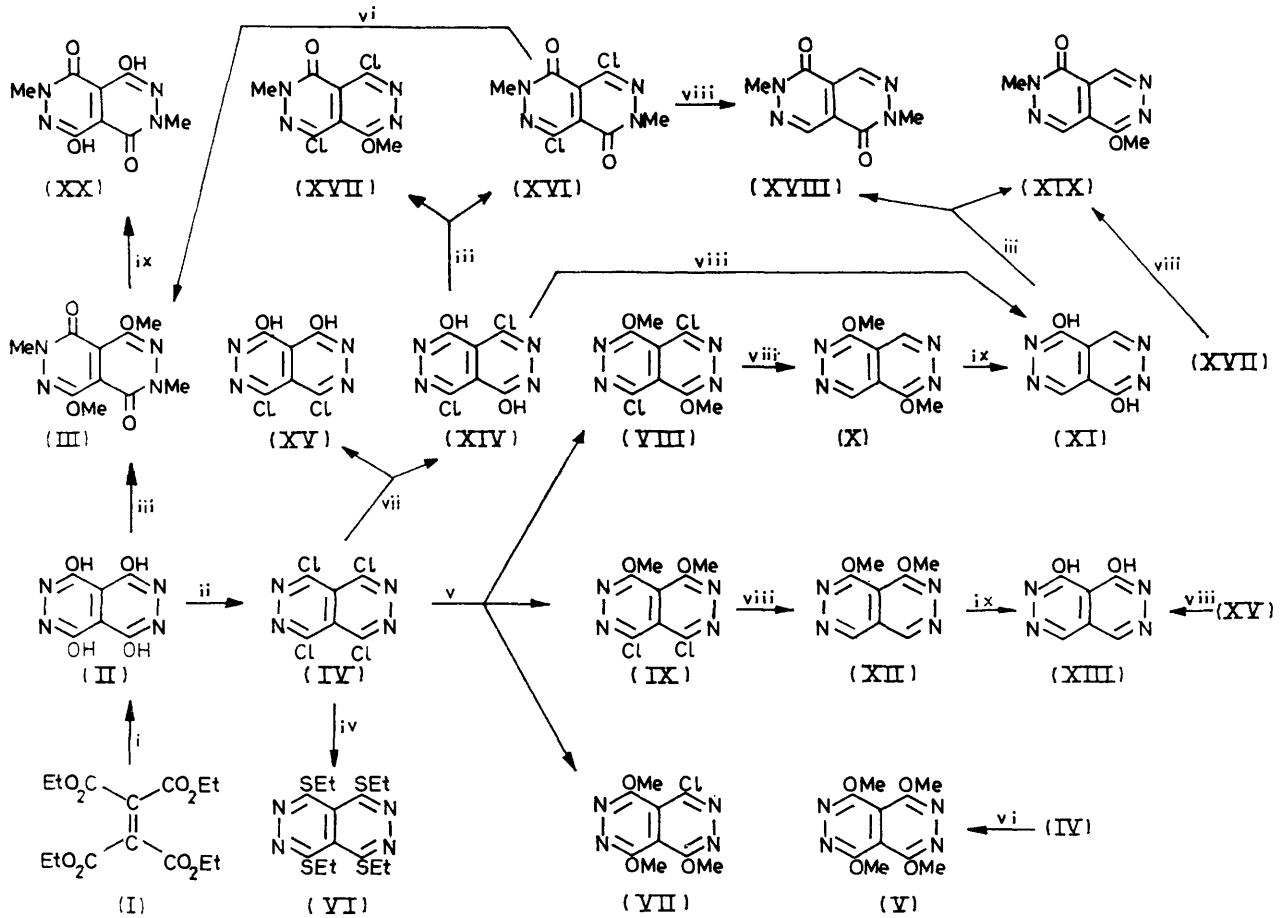
1,4,5,8-Tetrahydroxypyridazino[4,5-*d*]pyridazine (II), obtained by condensation of tetraethyl ethylenetetracarboxylate (I) with hydrazine, gave the 1,4,5,8-tetrachloro-derivative (IV) with PCl_5–$POCl_3$. The chlorine atoms of compound (IV) could be totally or partially displaced with nucleophiles. Sodium methoxide (2 mol. equiv.) yielded a mixture of two dimethoxy-dichloro-pyridazino[4,5-*d*]pyridazines from which 1,5- (XI) and 1,8-dihydroxypyridazino[4,5-*d*]pyridazine (XIII) were obtained by hydrogenation followed by acidic hydrolysis.

The alkaline hydrolysis of compound (IV) yielded a mixture of 1,5-dichloro-4,8-dihydroxy- (XIV) and a little amount of 1,8-dichloro-4,5-dihydroxy-pyridazino[4,5-*d*]pyridazine (XV).

Compounds (XI) and (XIV) reacted with diazomethane to give mixtures of the corresponding bis-*N*-methyl- and *NO*-dimethyl-derivatives, whereas compound (II) yielded 4,8-dimethoxy-2,6-dimethylpyridazino[4,5-*d*]-pyridazine-1,5(2*H*,6*H*)-dione (III).

We have briefly reported [1] the reactions of 1,4,5,8-tetrahydroxypyridazino[4,5-*d*]pyridazine (II) obtained by treatment of tetraethyl ethylenetetracarboxylate (I) with chloride–phosphoryl chloride mixture gave 1,4,5,8-tetrachloropyridazino[4,5-*d*]pyridazine (IV) in 36% yield. This gave the tetrasubstituted compounds (V)



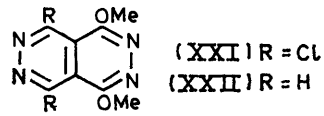
Reagents: i, N_2H_4; ii, PCl_5–$POCl_3$; iii, CH_2N_2; iv, NaSEt; v, NaOMe (2 mol. equiv. in PhMe); vi, NaOMe; vii, NaOH; viii, H_2–Pd/C; ix, HBr–AcOH.

hydrazine hydrate in refluxing methanol. Here we amplify that report and also describe other new pyridazino[4,5-*d*]pyridazines.

Treatment of compound (II) with a phosphorus penta- and (VI) in high yields upon treatment with methoxide or thioethoxide.

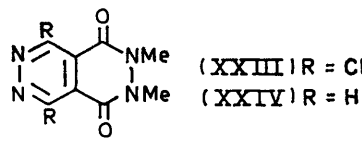
[1] G. Adembri, F. De Sio, and R. Nesi, *Ricerca Sci.*, 1967, **37**, 440.

Treatment of compound (IV) with sodium methoxide (2 mol. equiv.) in toluene [in methanol only the tetramethoxy-derivative (V) was obtained] gave a mixture from which the dichloro-dimethoxy-pyridazino[4,5-*d*]-pyridazines (VIII) and (IX) with a small amount of 1-chloro-4,5,8-trimethoxypyridazino[4,5-*d*]pyridazine (VII) were separated by preparative t.l.c. The structure of 1,4-dichloro-5,8-dimethoxypyridazino[4,5-*d*]-pyridazine (XXI) was excluded for compounds (VIII) and (IX) since on catalytic dehalogenation they failed to give the known 1,4-dimethoxypyridazino[4,5-*d*]-pyridazine (XXII)[2]; instead the dimethoxypyridazino[4,5-*d*]pyridazines (X) and (XII) respectively were formed. Compounds (X) and (XII) gave the corresponding dihydroxy-derivatives (XI) and (XIII) on hydrolysis with hydrobromic acid in acetic acid. The structures of all these compounds were established starting from compound (IV) as follows.



(XXI) R = Cl
(XXII) R = H

The alkaline hydrolysis of the tetrachloro-derivative (IV) afforded a mixture of compound (XIV) with a small amount of (XV); the separation of the two isomers was achieved by fractional precipitation from a hot acidic solution. When compound (XIV) was treated with an excess of diazomethane, the main product (90%) was the dimethyl-derivative (XVI) with a small amount of the isomer (XVII), whose purification was achieved by preparative t.l.c. Spectroscopic data of compounds (XVI) and (XVII) were consistent with structures of *NN*- and *NO*-dimethyl-derivatives respectively; their i.r. spectra show a strong band at 1670 cm^{-1} (ν_{CO}) and n.m.r. spectra exhibit a single peak at δ 3·66 p.p.m. (2 × N–CH_3) and two singlets at δ 4·3 (O–CH_3) and 3·85 p.p.m. (N–CH_3) respectively. Furthermore the 1,4-dioxo-structure (XXIII) was excluded for compound (XVI) since on catalytic dehalogenation it gave the dioxo-derivative (XVIII) which was different from 2,3-dimethylpyridazino[4,5-*d*]pyridazine-1,4(2*H*,3*H*)-dione[2] (XXIV):

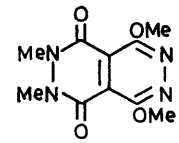


(XXIII) R = Cl
(XXIV) R = H

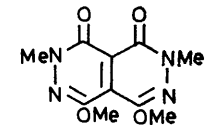
The i.r. spectrum of compound (XVIII) in CCl_4 suggests a centrosymmetric structure since a single band is present in the region of the stretching vibrations of carbonyl groups (1665 cm^{-1}). An *X*-ray analysis[3] of compound (XVI) confirmed that it was 4,8-dichloro-2,6-dimethylpyridazino[4,5-*d*]pyridazine-1,5(2*H*,6*H*)-dione; compound (XVIII) was, therefore, identified as 2,6-dimethylpyridazino[4,5-*d*]pyridazine-1,5(2*H*,6*H*)-dione. Consequently compounds (XIV) and (XVII) were formulated as 1,5-dichloro-4,8-dihydroxypyridazino[4,5-*d*]pyridazine and 4,8-dichloro-5-methoxy-2-methylpyridazino[4,5-*d*]-pyridazin-1(2*H*)-one respectively. The hydroxy-derivative (XI) was then assigned the structure of 1,5-dihydroxypyridazino[4,5-*d*]pyridazine since it could be obtained also by catalytic dehalogenation of compound (XIV), and on the basis of this assignment compounds (X) and (VIII) were formulated as 1,5-dimethoxy- and 1,5-dichloro-4,8-dimethoxy-pyridazino[4,5-*d*]pyridazine respectively. Therefore compounds (XII) and (IX), for which the structures (XXII) and (XXI) were previously discarded, are 1,8-dimethoxy- and 1,8-dichloro-4,5-dimethoxy-pyridazino[4,5-*d*]pyridazine respectively; consequently compound (XIII) was assigned the structure of 1,8-dihydroxypyridazino[4,5-*d*]pyridazine and compound (XV) was identified as 1,8-dichloro-4,5-dihydroxypyridazino[4,5-*d*]pyridazine since it yielded compound (XIII) on catalytic dehalogenation.

Methylation of compound (XI) with diazomethane afforded a mixture of compound (XVIII) and of an isomer (XIX) which was formulated as 5-methoxy-2-methylpyridazino[4,5-*d*]pyridazin-1(2*H*)-one since it could be obtained also from compound (XVII) on catalytic dehalogenation.

The tetrahydroxy-derivative (II) reacted with diazomethane to yield a yellow product whose analytical data are in agreement with a tetramethyl-derivative. Its n.m.r. spectrum, showing two singlets (in the ratio 1 : 1) at δ 3·99 (2 × O–CH_3) and 3·75 p.p.m. (2 × N–CH_3), is consistent with the formulation of this compound as a bis-*O*-methyl-bis-*N*-methyl-derivative but it does not allow a decision among structures such as (III), (XXV), and (XXVI) even if the i.r. spectrum, showing a single band at 1660 cm^{-1} (in CCl_4) for the stretching vibrations of the two carbonyl groups, suggests the centrosymmetric structure of 4,8-dimethoxy-2,6-dimethylpyridazino-[4,5-*d*]pyridazine-1,5(2*H*,6*H*)-dione (III). This suggestion was confirmed by synthesis from the dichloro-derivative (XVI) and sodium methoxide.



(XXV)



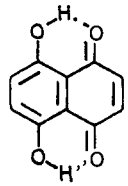
(XXVI)

Hydrolysis of compound (III) with hydrobromic acid in acetic acid yielded 3,7-dimethylpyridazino[4,5-*d*]-pyridazine-1,4,5,8(2*H*,3*H*,6*H*,7*H*)-tetraone (XX). Its i.r. spectrum exhibits a weak broad band between 3300 and 2800 cm^{-1} (maximum at 3040 cm^{-1}) and a strong band at 1605 cm^{-1}. These frequencies are in complete agreement with those of OH and CO groups of 5,8-di-

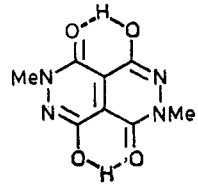
[2] G. Adembri, F. De Sio, R. Nesi, and M. Scotton, *J. Chem. Soc.* (*C*), 1968, 2857.

[3] C. Sabelli, P. Tangocci, and P. F. Zanazzi, *Acta Cryst.*, in the press.

hydroxynaphthoquinone (broad band centred at 2920 cm^{-1} and a strong band at 1608 cm^{-1}) which was formulated as (XXVII).[4] From this consideration we conclude that compound (XX) exists in the chelated dihydroxy-form (XXa).



(XXVII)



(XXa)

EXPERIMENTAL

Unless otherwise stated, i.r. spectra were measured for potassium bromide discs with a Perkin-Elmer 457 spectrometer and ^1H n.m.r. spectra were recorded for solutions in deuteriochloroform with a Varian A-56/60 instrument; chemical shifts are reported in p.p.m. downfield from internal tetramethylsilane. U.v. spectra were determined with a Cary 14 spectrophotometer. Silica gel plates (Merck F_{254}) were used for analytical and preparative t.l.c. Light petroleum refers to the fraction b.p. 75—120°.

1,4,5,8-*Tetrahydroxypyridazino*[4,5-d]*pyridazine* (II).—Hydrazine hydrate (98%; 50 ml) was added dropwise with stirring to a boiling solution of tetraethyl ethylenetetracarboxylate (I) (50 g) in methanol (175 ml), and the reaction mixture was refluxed for 7 h. After the mixture had been set aside overnight, the yellow product was filtered off, washed with hot methanol (2 × 50 ml), and dissolved in hot water (340 ml); acetic acid (30%; 100 ml) was added with vigorous stirring and the mixture was heated at 80—90° for 8 h. After cooling, the *tetrahydroxy-derivative* (II) (12·5 g), as yellow-orange solid, was filtered off; a further crop (3 g) was obtained from the mother liquors; total yield 15·5 g (50%), m.p. >340° (after sublimation at 250°/0·05 mmHg and recrystallisation from dimethylformamide) (Found: C, 36·8; H, 2·2; N, 28·8. $C_6H_4N_4O_4$ requires C, 36·8; H, 2·0; N, 28·6%), $\nu_{max.}$ 3140s, br, 1640s, 1560m, 1450s, 1430s, 1345m, 1290s, 1210m, 990w, 950s, 870w, 790m, 762s, 685m, 675w, 511w, 436m, and 408w cm^{-1}; $\lambda_{max.}$ (dimethylformamide) 280 and 434 nm (log ε 3·65 and 3·62).

1,4,5,8-*Tetrachloropyridazino*[4,5-d]*pyridazine* (IV).—Finely ground tetrahydroxy-derivative (II) (4 g; previously dried at 120°), phosphorus pentachloride (34 g), and freshly distilled phosphoryl chloride (250 ml) were refluxed at 130—140° (bath) for 24 h. After phosphoryl chloride had been distilled off under reduced pressure, the phosphorus pentachloride was removed by sublimation; the residue was poured on crushed ice, filtered, and dried *in vacuo* (P_2O_5 and KOH). Trituration of the product with anhydrous acetone gave *compound* (IV) (2 g, 36%) as pale yellow solid suitable for several preparative purposes; a pure specimen, m.p. >300° was prepared by several recrystallisations from the same solvent (Found: C, 26·9; Cl, 51·9; N, 20·8. $C_6Cl_4N_4$ requires C, 26·7; Cl, 52·6; N, 20·8%) $\nu_{max.}$ 1400m, 1340m, 1322w, 1285s, 1025w, 845s, 660w, and 640m cm^{-1}, $\lambda_{max.}$ (dioxan) 285, 290sh, 310sh, 324, and 337sh nm (log ε 3·96, 3·95, 3·78, 3·69, and 3·54).

1,4,5,8-*Tetramethoxypyridazino*[4,5-d]*pyridazine* (V).—Compound (IV) (0·4 g) was added to a stirred solution of sodium (0·2 g) in anhydrous methanol (20 ml) and refluxed for 3 h. After evaporation of the solvent, the solid residue was poured into cold water (10 ml) and filtered to give a white *compound* (0·34 g, 91%), m.p. 288—289° (from benzene) (Found: C, 47·7; H, 5·0; N, 22·3. $C_{10}H_{12}N_4O_4$ requires C, 47·6; H, 4·8; N, 22·2%), $\nu_{max.}$ 3030w, 3005w, 2960w, 1510s, 1475m, 1465s, 1450m, 1380s, 1185w, 1045s, 1025s, 915w, 760m, and 735m cm^{-1}; $\lambda_{max.}$ (MeOH) 217, 222sh, 268, 321, 336, and 351 nm (log ε 4·07, 3·95, 3·88, 3·64, 3·86, and 3·82), δ 4·22 (s).

1,4,5,8-*Tetraethoxypyridazino*[4,5-d]*pyridazine*.— Treated as above, compound (IV) (1 g) and sodium ethoxide gave white *crystals* (1 g, 87%), m.p. 259—260° (from benzene) (Found: C, 54·7; H, 6·7; N, 18·2. $C_{14}H_{20}N_4O_4$ requires C, 54·5; H, 6·5; N, 18·2%).

1,4,5,8-*Tetra*(*ethylthio*)*pyridazino*[4,5-d]*pyridazine* (VI).—A solution of sodium ethyl sulphide (0·38 g) in anhydrous ethanol (10 ml) was added dropwise to a stirred suspension of compound (IV) (0·28 g) in the same solvent (20 ml) and the mixture was refluxed for 3 h. Removal of the solvent *in vacuo* gave a solid which was triturated with water and extracted with chloroform to yield a yellow *product* (0·35 g, 90%), m.p. 245—247° (after several recrystallisations from ethyl acetate) (Found: C, 45·4; H, 5·2; N, 15·0; S, 34·2. $C_{14}H_{20}N_4S_4$ requires C, 45·2; H, 5·4; N, 15·0; S, 34·4%), $\nu_{max.}$ 2980w, 2930w, 2865w, 1445m, 1430s, 1285s, 1240m, 840m, and 585m cm^{-1}; $\lambda_{max.}$ ($CHCl_3$) 274, 370, and 410sh nm (log ε 3·8, 4·2, and 3·81).

Reaction of 1,4,5,8-*Tetrachloropyridazino*[4,5-d]*pyridazine with Sodium Methoxide in Toluene*.—A suspension of compound (IV) (0·5 g) and sodium methoxide (0·205 g, 2 mol) in anhydrous toluene (40 ml) was stirred at 60—70° for 4 h. Removal of the solvent left a residue which was extracted with chloroform to give a pale yellow solid (0·45 g); t.l.c. in chloroform–benzene (2 : 3 v/v) showed three spots. Recrystallisation from chloroform (12 ml) gave 1,5-*dichloro*-4,8-*dimethoxypyridazino*[4,5-d]*pyridazine* (VIII) (0·08 g), m.p. 218—219° (decomp.) (from carbon tetrachloride) (Found: C, 36·6; H, 2·25; Cl, 27·5; N, 21·4. $C_8H_6Cl_2N_4O_2$ requires C, 36·8; H, 2·3; Cl, 27·2; N, 21·5%), $\nu_{max.}$ 3030w, 3005w, 2955w, 1495s, 1470m, 1443m, 1435w, 1390s, 1340s, 1262m, 1190w, 1105w, 1030s, 900m, 800m, 735m, 700m, and 675w cm^{-1}, $\lambda_{max.}$ (MeOH) 205, 277, 316, 329, and 342 nm (log ε 4·31, 3·91, 3·70, 3·80, and 3·73).

The solid recovered from the chloroform mother liquors was resolved on preparative t.l.c. plates with chloroform–benzene (2 : 3 v/v) as developer, to give a second crop (0·07 g) of compound (VIII), 1,8-*dichloro*-4,5-*dimethoxypyridazino*-[4,5-d]*pyridazine* (IX) (0·13 g), m.p. 179—181° (from light petroleum) (Found: C, 36·7; H, 2·3; Cl, 27·3; N, 21·6. $C_8H_6Cl_2N_4O_2$ requires C, 36·8; H, 2·3; Cl, 27·2; N, 21·5%), $\nu_{max.}$ 2990w, 2945w, 1555m, 1482s, 1465m, 1445w, 1435w, 1380s, 1320w, 1055w, 998s, 886w, 808w, 738w, and 692w cm^{-1}; $\lambda_{max.}$ (MeOH) 205, 250sh, 275, 285sh, 317, 330, and 343 nm (log ε 4·28, 3·56, 3·93, 3·88, 3·69, 3·8, and 3·72) and a small amount of 1-*chloro*-4,5,8-*trimethoxypyridazino*-[4,5-d]*pyridazine* (VII), m.p. 202—203° (from light petroleum) (Found: C, 42·3; H, 3·5; Cl, 13·7; N, 22·0. $C_9H_8ClN_4O_3$ requires C, 42·2; H, 3·5; Cl, 13·8; N, 21·8%), $\nu_{max.}$ 2990w, 2955w, 1570w, 1495s, 1470m, 1460m, 1440w, 1375s, 1180w, 1025s, 995m, 990w, 755m, and 710m cm^{-1}; $\lambda_{max.}$ (MeOH) 202, 240sh, 278, 322sh, 337, and 345sh nm (log ε 4·35, 3·5, 3·85, 3·61, 3·78, and 3·74).

[4] D. Hadzi and N. Sheppard, *Trans. Faraday Soc.*, 1954, **50**, 911.

1,5-*Dimethoxypyridazino*[4,5-d]*pyridazine* (X).—Hydrogenation of compound (VIII) (0·2 g) in anhydrous dioxan (50 ml) containing triethylamine (0·25 ml) and palladium–charcoal (5%; 0·2 g) at room temperature and atmospheric pressure led to the uptake of *ca.* 2 mol. equiv. of hydrogen in 2 h. Removal of the catalyst and solvent left a residue which was treated with aqueous sodium hydroxide and extracted with chloroform. Evaporation of the dried chloroform extracts yielded *compound* (X) (0·1 g, 68%), m.p. 206—208° (after sublimation at 90°/0·05 mmHg and recrystallisation from water) (Found: C, 49·8; H, 4·2; N, 28·9. $C_8H_8N_4O_2$ requires C, 50·0; H, 4·2; N, 29·1%), $\nu_{max.}$ 3015w, 2960w, 2915w, 2850w, 1500m, 1475s, 1445m, 1375s, 1225m, 1065s, 995s, 910m, 880w, 810m, 740w, 730m, 630m, 625m, 535m, and 340w cm^{-1}; $\lambda_{max.}$ (H_2O) 256, 262, 272sh, 293sh, 301, and 314 nm (log ε 3·78, 3·79, 3·68, 3·69, 3·83, and 3·81); δ 4·38(s) and 9·57(s).

1,8-*Dimethoxypyridazino*[4,5-d]*pyridazine* (XII).—Hydrogenation of compound (IX) (0·16 g) under the same conditions used for compound (VIII) yielded 1,8-*dimethoxypyridazino*[4,5-d]*pyridazine* (XII) (0·09 g, 76%), m.p. 210° (decomp.) (after sublimation at 100°/0·05 mmHg and recrystallisation from benzene–light petroleum) (Found: C, 50·2; H, 4·3; N, 28·9. $C_8H_8N_4O_2$ requires C, 50·0; H, 4·2; N, 29·1%), $\nu_{max.}$ 3040w, 3015w, 2990w, 2950w, 1605w, 1590s, 1515s, 1460s, 1370s, 1185w, 1135m, 1070w, 995s, 975m, 810w, 695w, and 665m cm^{-1}; $\lambda_{max.}$ (H_2O) 228, 254, 266sh, 295sh, 304, and 316 nm (log ε 3·79, 3·84, 3·70, 3·70, 3·83, and 3·80).

1,5-*Dihydroxypyridazino*[4,5-d]*pyridazine* (XI).—(*a*) Hydrolysis of compound (X) (0·05 g) in acetic acid (2 ml) and hydrobromic acid (48%; 0·3 ml) at reflux temperature for 1 h gave *compound* (XI) (0·035 g, 82%), m.p. >340° (from water) (Found: C, 44·2; H, 2·6; N, 34·1. $C_6H_4N_4O_2$ requires C, 43·9; H, 2·5; N, 34·1%), $\nu_{max.}$ 3300—2500m, vbr, 1645s, 1610s, 1570m, 1440m, 1250m, 1230m, 1120w, 980w, 790s, 750m, 590m, and 575m cm^{-1}; $\lambda_{max.}$ (H_2O) 210, 262, 270, 279, 320, 334, and 351 nm (log ε 4·17, 3·89, 3·91, 3·78, 3·75, 3·9, and 3·81).

(*b*) Compound (XIV) (0·2 g) was dissolved in aqueous sodium hydroxide (1N; 35 ml) and methanol (16 ml) was added, followed by palladium–charcoal (5%; 0·2 g). The mixture was hydrogenated at atmospheric pressure and room temperature until 2 mol. equiv. of the gas had been consumed. The solution, after removal of the catalyst, was concentrated under reduced pressure and acidified (pH 1) with concentrated hydrochloric acid to give a pale yellow product (0·1 g, 72%) identical (i.r. spectrum) with material prepared by method (*a*).

1,8-*Dihydroxypyridazino*[4,5-d]*pyridazine* (XIII).—(*a*) Hydrolysis of compound (XII) (0·03 g) was carried out as described for compound (X) to give the *dihydroxy-derivative* (XIII) (0·02 g, 78%), m.p. >300° (from water) (Found: C, 43·8; H, 2·4; N, 34·2. $C_6H_4N_4O_2$ requires C, 43·9; H, 2·5; N, 34·1%), $\nu_{max.}$ 3300—2500m, vbr, 1690s, 1600m, 1580m, 1535w, 1465w, 1390w, 1230m, 1155w, 1130m, 1105m, 925w, 870m, 830m, 810m, 685w, 670w, 580w, and 510m cm^{-1}; $\lambda_{max.}$ (H_2O) 212, 245, and 325 nm (log ε 3·87, 4·03, and 3·81).

(*b*) Hydrogenation of compound (XV) (0·07 g) under the same conditions used for compound (XIV) yielded a pale yellow product (0·03 g) identical (i.r. spectrum) with material prepared with method (*a*).

Alkaline Hydrolysis of Compound (IV).—Compound (IV) (1·3 g) in aqueous sodium hydroxide (2N; 50 ml) was stirred at 60—70° for 2 h; the resulting solution was kept overnight in the refrigerator to give yellow crystals (1·2 g) which were dissolved in hot water (30 ml). Acidification with concentrated hydrochloric acid (pH 1) precipitated a solid which was filtered off whilst hot and washed freely with hot methanol (Soxhlet, 12 h) to yield 1,5-*dichloro*-4,8-*dihydroxypyridazino*[4,5-d]*pyridazine* (XIV) (0·65 g). The product was purified for analysis by dissolution of a sample in aqueous sodium hydroxide, filtration, and reprecipitation of compound (XIV) with concentrated hydrochloric acid as a pale yellow powder, m.p. >340° (Found: C, 30·9; H, 0·8; Cl, 30·4; N, 24·0. $C_6H_2Cl_2N_4O_2$ requires C, 30·9; H, 0·9; Cl, 30·5; N, 24·0%), $\nu_{max.}$ 3300—2500m, vbr, 1675s, 1530w, 1425m, 1305w, 1245m, 1185w, 975m, 835m, 790m, 730m, and 635w cm^{-1}.

The acidic mother liquors (pH 1) were cooled and then set aside overnight in a refrigerator to give a crude product (0·15 g) from which 1,8-*dichloro*-4,5-*dihydroxypyridazino*[4,5-d]*pyridazine* (XV) was obtained by several acid–base precipitations, m.p. >300° (from water containing a few drops of hydrochloric acid) (Found: C, 30·6; H, 1·1; Cl, 30·2; N, 23·8. $C_6H_2Cl_2N_4O_2$ requires C, 30·9; H, 0·9; Cl, 30·5; N, 24·0%), $\nu_{max.}$ 3300—2500m, vbr, 1735s, 1705m, 1630w, 1560w, 1535m, 1465w, 1205w, 1185m, 1155w, 1120w, 925m, 840w, 810m, 760m, and 520m cm^{-1}.

Methylation of Compound (XIV) *with Diazomethane*.—A suspension of compound (XIV) (1 g) in ethyl ether (120 ml) and methanol (40 ml) was treated with an excess of diazomethane in ether and set aside overnight. Filtration of the reaction mixture yielded 4,8-*dichloro*-2,6-*dimethylpyridazino*[4,5-d]*pyridazino*-1,5(2H,6H)-*dione* (XVI) as yellow needles, m.p. 319—321° (from dioxan) (Found: C, 36·7; H, 2·3; Cl, 26·9; N, 21·6. $C_8H_6Cl_2N_4O_2$ requires C, 36·8; H, 2·3; Cl, 27·2; N, 21·5%), $\nu_{max.}$ 3000w, 2950w, 1665s, 1550w, 1505m, 1400w, 1350w, 1335w, 1250m, 1080m, 1040m, 910m, 790m, 750m, 690w, and 615m cm^{-1}; $\lambda_{max.}$ (MeOH) 229, 287, 295sh, 360sh, 378, and 398 nm (log ε 3·97, 3·78, 3·6, 3·7, 3·9, and 3·88). Evaporation of the solution under reduced pressure left a solid residue from which tarry material was eliminated by preparative t.l.c. in chloroform–benzene (2 : 3 v/v). A further preparative t.l.c. in ether gave traces of compound (XVI) and 4,8-*dichloro*-5-*methoxy*-2-*methylpyridazino*[4,5-d]*pyridazin*-1(2H)-*one* (XVII) (0·08 g), m.p. 196—198° (if immersed at *ca.* 185°) * (from methanol) (Found: C, 36·8; H, 2·4; Cl, 27·0; N, 21·4. $C_8H_6Cl_2N_4O_2$ requires C, 36·8; H, 2·3; Cl, 27·2; N, 21·5%), $\nu_{max.}$ 2970w, 1670s, 1550m, 1530m, 1490w, 1450m, 1360s, 1325s, 1250m, 1090w, 1025s, 945m, 890w, 780m, 740m, 720w, 680m, 660m, 550w, and 470w cm^{-1}; $\lambda_{max.}$ (MeOH) 279, 284, 352, and 365sh nm (log ε 3·85, 3·86, 3·83, and 3·80).

2,6-*Dimethylpyridazino*[4,5-d]*pyridazine*-1,5(2H,6H)-*dione* (XVIII).—Hydrogenation of compound (XVI) (0·2 g) in anhydrous dioxan (150 ml) containing triethylamine (0·25 ml) and palladium–charcoal (5%; 0·2 g) carried out essentially as described for compound (VIII) gave *compound* (XVIII) (0·1 g, 68%), m.p. 246—248° (after sublimation at 90°/0·03 mmHg and recrystallisation from methanol) (Found: C, 49·9; H, 4·2; N, 29·2. $C_8H_8N_4O_2$ requires C, 50·0; H, 4·2; N, 29·1%), $\nu_{max.}$ 3055w, 2955w, 2920w, 1640s, 1535m, 1375w, 1290m, 1090w, 1010m, 940w, 915m,

* Like other methoxy-pyridazines (M. Tisler and B. Stanovnik, *Adv. Heterocyclic Chem.*, 1968, **9**, 265) compound (XVII) is converted into compound (XVI) on heating.

750m, 695m, 625w, and 545m cm^{-1}, $\lambda_{max.}$ (H_2O) 217, 266, 275, 282sh, 328sh, 340, and 357 nm (log ε 4·12, 3·77, 3·80, 3·65, 3·79, 3·97, and 3·97).

5-*Methoxy*-2-*methylpyridazino*[4,5-d]*pyridazin*-1(2H)-*one* (XIX).—Treated as above, compound (XVII) (0·15 g) gave a crude product from which *compound* (XIX) (0·07 g; 64%) was isolated by preparative t.l.c. [benzene–chloroform (1 : 3)], m.p. 194—195° (after sublimation at 80°/0·05 mmHg and recrystallisation from light petroleum) (Found: C, 49·8; H, 4·4; N, 29·1. $C_8H_8N_4O_2$ requires C, 50·0; H, 4·2; N, 29·1%), $\nu_{max.}$ 3055w, 2945w, 1660s, 1590m, 1565m, 1460s, 1410w, 1355s, 1275m, 1240w, 1075m, 1030s, 940m, 925w, 735m, 615w, 545m, and 452w cm^{-1}, $\lambda_{max.}$ (H_2O) 210sh, 263sh, 268, 290, 321, and 330sh nm (log ε 4·1, 3·81, 3·84, 3·62, 3·92, and 3·87).

Methylation of Compound (XI) *with Diazomethane.*—A suspension of compound (XI) (0·1 g) in ethyl ether (30 ml) and methanol (10 ml) was treated with an excess of diazomethane in ether and set aside overnight. Filtration of the reaction mixture yielded compound (XVIII) (0·03 g) identical (m.p. and i.r. spectrum) with material prepared from compound (XVI) as described above; the solid recovered from the mother liquors was resolved into two components by preparative t.l.c. with benzene–chloroform (3 : 2 v/v) as developer. The faster-running band gave a second crop (0·02 g) of compound (XVIII) and the slower gave compound (XIX) (0·03 g) identical (m.p. and i.r. spectrum) with material prepared from compound (XVII) as described above.

4,8-*Dimethoxy*-2,6-*dimethylpyridazino*[4,5-d]*pyridazine*-1,5(2H,6H)-*dione* (III).—(*a*) Methylation of the tetrahydroxy-derivative (II) (0·5 g) carried out as for compound (XI) yielded a brown-yellow solid which was digested with 1N-sodium hydroxide solution and extracted with chloroform. Evaporation of the solvent gave *compound* (III) (0·5 g, 78%), m.p. 306—307° (after several recrystallisations from ethyl acetate) (Found: C, 47·5; H, 4·6; N, 22·3. $C_{10}H_{12}N_4O_4$ requires C, 47·6; H, 4·8; N, 22·2%), $\nu_{max.}$ 2995w, 2950w, 1645s, 1530s, 1450m, 1400m, 1382m, 1320w, 1270m, 1180m, 1100m, 1070m, 1020m, 900w, 755m, 735w, and 625m cm^{-1}; $\lambda_{max.}$ (dimethylformamide) 269, 278, 287sh, 371, 390, and 412 nm (log ε 3·74, 3·72, 3·52, 3·71, 3·90, and 3·89), δ 3·75 (6H, s, 2 × N–CH_3) and 3·99 (6H, s, 2 × O–CH_3).

(*b*) Compound (XVI) (0·1 g) was added to a solution of sodium (0·1 g) in anhydrous methanol (6 ml) and refluxed with stirring for 4 h. Removal of the solvent left a residue which was treated with water to give compound (III) (0·07 g, 72%) identical (m.p. and i.r. spectrum) with material prepared by method (*a*).

3,7-*Dimethylpyridazino*[4,5-d]*pyridazine*-1,4,5,8-(2H,3H,6H,7H)-*tetraone* (XX).—Hydrolysis of compound (III) (0·4 g) in acetic acid (20 ml) and hydrobromic acid (48%; 6 ml) at reflux temperature for 1 h gave *compound* (XX) (0·32 g, 90%), m.p. >300° (from dimethylformamide) (Found: C, 43·0; H, 3·7; N, 25·0. $C_8H_8N_4O_4$ requires C, 42·9; H, 3·6; N, 25·0%), $\nu_{max.}$ 3300—2800w, vbr, 1605s, 1445s, 1405w, 1345m, 1250s, 1120w, 1075m, 955m, 905m, 790m, 755m, 720w, 680w, 640m, and 510w cm^{-1}; $\lambda_{max.}$ (dimethylformamide) 268, 281, 290sh, 365sh, 384, 406, and 450sh nm (log ε 3·65, 3·64, 3·56, 3·60, 3·80, 3·84, and 3·23).

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