[1,4]Benzodioxinopyridazines

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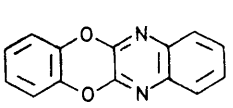
3-Chloro[1.4]benzodioxino[2,3-*c*]pyridazine was prepared from 3,4,6-trichloropyridazine and catechol and was catalytically reduced to [1,4]benzodioxino[2,3-*c*]pyridazine. Attempted nucleophilic displacement reactions of the chloro-compound with alkoxide ions or with amines generally cleaved the dioxin ring preferentially, though with some amines the chloro-substituent was replaced without ring cleavage. [1,4]Benzodioxino[2.3-*c*]-pyridazine and [1,4]benzodioxino[2.3-*b*]quinoxaline were less reactive; the dioxin ring was not attacked on heating with morpholine but ring cleavage was effected by boiling methanolic sodium methoxide. The preparation of [1,4]benzodioxino[2,3-*d*]pyridazine by way of the 1-chloro-derivative is described.

TRICHLOROPYRIDAZINES are highly reactive and have been used extensively for the synthesis of pyridazinobenzothiazines,[1,2] pyridazinobenzoxazines,[3] and dipyridazinodithiins.[4] 2,3-Dichloroquinoxaline shows similar reactivity and has been condensed with catechol [5] to give [1,4]benzodioxino[2,3-*b*]quinoxaline (I). These results suggested that trichloropyridazines might similarly form benzodioxinopyridazines. The condensation of catechol with tetrachloropyrazine to give the analogous 2,3-dichloro[1,4]benzodioxino[2,3-*b*]pyrazine has been reported recently.[6]

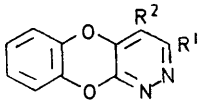
Condensation of the disodium salt of catechol with 3,4,6-trichloropyridazine gave 3-chloro[1,4]benzodioxino-[2,3-*c*]pyridazine (*II*; $R^1 = Cl$, $R^2 = H$) in 50% yield. Direct condensation with catechol in a ketone solvent in the presence of potassium carbonate gave a similar result. Catalytic hydrogenation of the product in the presence of a base gave the parent heterocycle (*II*; $R^1 = R^2 = H$). 4-Nitrocatechol and 3-methoxycatechol reacted similarly with 3,4,6-trichloropyridazine, and in each case only one product was detected. These compounds are tentatively formulated as 6-nitro- and 5-methoxy-derivatives, respectively: it is assumed that, since only one reaction orientation is observed, the more basic aryl oxide group (*m*- to nitro-, *o*- to methoxy-) would initially attack the reactive 4-position of the pyridazine ring.

[1] F. Yoneda, T. Ohtaka, and Y. Nitta, *Chem. and Pharm. Bull.* (*Japan*), 1965, **13**, 580.
[2] O. R. Rodig, R. E. Collier, and R. K. Schlatzer, *J. Org. Chem.*, 1964, **29**, 2652.
[3] V. G. Nyrkova, T. V. Gortinskaya, and M. N. Shchukina, *Zhur. org. Khim.*, 1965, **1**, 1688.
[4] M. Kuzuya and K. Kaji, *Chem. and Pharm. Bull.* (*Japan*), 1970, **18**, 2420.
[5] F. Kehrmann and C. Bener, *Helv. Chim. Acta*, 1925, **8**, 16.
[6] A. H. Gulbenk, U.S.P., 3,663,543/1972.

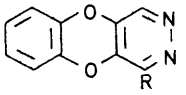
Similarly 3,4,5-trichloropyridazine condensed with catechol to give 1-chloro[1,4]benzodioxino[2,3-*d*]pyridazine (III; R = Cl), which was catalytically reduced to



(I)



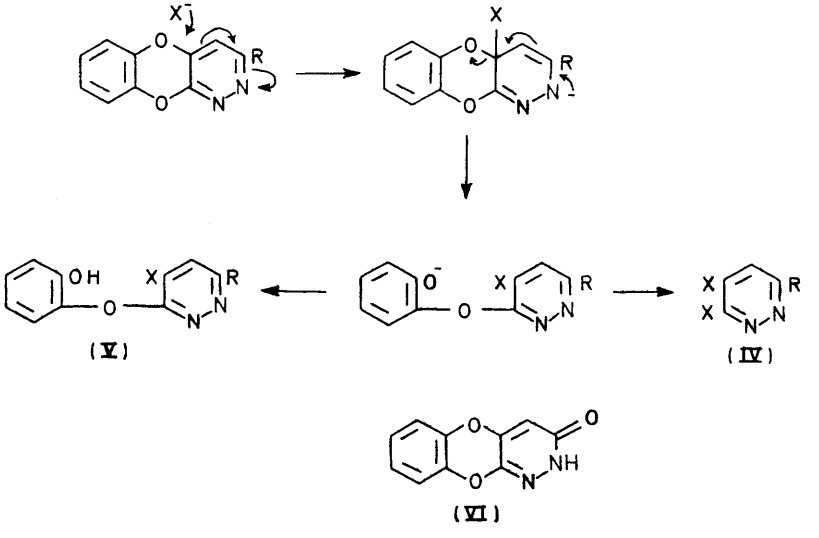
(II)



(III)

the parent heterocycle (III; R = H). No isomeric chloro-compound was detected; indeed the alternative product (II; R^1 = H, R^2 = Cl) would have been reduced to the compound (II; R^1 = R^2 = H) already described.

Nucleophilic displacement reactions of the chloro-compound (II; R^1 = Cl, R^2 = H) were examined in the hope of preparing compounds of interest for pharmacological testing. Treatment with boiling methanolic sodium methoxide, however, unexpectedly gave 3-chloro-5,6-dimethoxypyridazine (IV; R = Cl, X = OMe). Reaction at −70° gave an intermediate chloro-(*o*-hydroxyphenoxy)methoxypyridazine (V; R = Cl, X = OMe) or its isomer (X and HO·C_6H_4·O interchanged).



(V) (IV) (VI)

The former structure is preferred because 4-substituents in a pyridazine system are generally more reactive than 3-substituents in nucleophilic displacements.[7]

Although the occurrence of ring cleavage rather than halogen displacement was unexpected it is not inconsistent with earlier work. Thus the reactivity of 3-chloro-pyridazines is reduced by electron-donating substituents[8] and the dioxin ring should show this effect strongly. Diaryl ethers are only cleaved by alkali under drastic conditions[9] but, when electron-withdrawing groups are present, cleavage by alkalis or amines occurs more easily;[10] pyridazine ring systems show a similar effect, *e.g.* 4-phenoxycinnoline reacts with amines to give aminocinnolines.[11] In aromatic compounds, reaction with amines may displace either chloro- or phenoxy-substituents according to which is activated by *o*- or *p*-nitro-groups.[12]

Treatment of the chloro-compound (II; R^1 = Cl, R^2 = H) with potassium benzyl oxide in benzyl alcohol similarly gave 2,3-bisbenzyloxy-6-chloropyridazine (IV; R = Cl, X = O·CH_2Ph) and the product formed from it by *O*- ⟶ *N*-benzyl rearrangement, 2-benzyl-4-benzyloxy-6-chloropyridazin-3(2*H*)-one.[13] Catalytic hydrogenation of 2,3-bisbenzyloxy-6-chloropyridazine gave 6-chloropyridazine-3,4-diol (IV; R = Cl, X = OH) as a pyridazinone tautomer.

In the hope of displacing the 3-chloro-substituent of (II; R^1 = Cl, R^2 = H) without cleaving the ring, alcoholysis was examined. The chloro-compound was unaffected by boiling with methanol, even in the presence of sodium carbonate, but, on boiling with n-hexanol, [1,4]-benzodioxino[2,3-*c*]pyridazin-3-one (VI) was obtained in low yield. Although dry hexanol was used, the product may have been formed by reaction with traces of water or by alcoholysis followed by thermal dealkylation of the 3-hexyloxy-compound.

When the chloro-compound (II; R^1 = Cl, R^2 = H) was heated with diethylamine, benzylmethylamine, or *N*-methylpiperazine, the corresponding amine (II; R^1 = NR_2, R^2 = H) was obtained by displacement of

[7] R. S. Fenton, J. K. Landquist, and S. E. Meek, *J.C.S. Perkin I*, 1972, 2323; *cf.* J. K. Landquist and S. E. Meek, *ibid.*, p. 2735.

[8] R. S. Fenton, J. K. Landquist, and S. E. Meek, *J. Chem. Soc.* (*C*), 1971, 1536.

[9] K. H. Meyer and F. Bergins, *Ber.*, 1941, **47**, 3158; R. Amatatou and S. Araki, *J. Chem. Soc. Japan*, 1931, **52**, 484.

[10] D. L. Fox and E. E. Turner, *J. Chem. Soc.*, 1930, 1115.

[11] J. R. Keneford, K. Schofield, and J. C. E. Simpson, *J. Chem. Soc.*, 1948, 358.

[12] R. J. W. Le Fèvre, S. L. M. Saunders, and E. E. Turner, *J. Chem. Soc.*, 1927, 1168.

[13] *Cf.* G. W. H. Cheeseman and R. A. Goodwin, *J. Chem. Soc.* (*C*), 1971, 2973, 2977.

the halide. In contrast, heating with pyrrolidine, piperidine, or morpholine (under reflux) effected ring cleavage to give the chloro-compound (V; R = Cl, X = NR_2). Prolonged heating with morpholine in an autoclave, however, formed 3,4,6-trimorpholinopyridazine. Landquist and his co-workers [7] have shown that vigorous conditions are similarly required for the preparation of this trimorpholinopyridazine from the 3,4,6-trichloro-compound through 3,6-dichloro-4-morpholinopyridazine.

[1,4]Benzodioxino[2,3-*c*]pyridazine was markedly less susceptible to ring cleavage by nucleophiles than its 3-chloro-derivative. The parent compound was unchanged by long heating with morpholine; with boiling methanolic sodium methoxide only ring opening occurred giving 3-(2-hydroxyphenoxy)-4-methoxypyridazine (V; R = H, X = OMe).

Kehrmann and Bener [5] prepared [1,4]benzodioxino-[2,3-*b*]quinoxaline (I) by prolonged heating of 2,3-dichloroquinoxaline with a large excess of catechol at 200 °C. We obtained this product conveniently and in high yield by condensation of catechol with the dichloro-compound in boiling diethyl ketone in the presence of potassium carbonate. Treatment of the dioxinoquinoxaline with sodium methoxide or ethoxide in the boiling alcohol gave the 2,3-dialkoxyquinoxaline but, with less than 2 mol. equiv. of sodium ethoxide, 2-ethoxy-3-(2-hydroxyphenoxy)quinoxaline was isolated in low yield. The dioxinoquinoxaline was unchanged by heating with morpholine or *N*-methylpiperazine.

EXPERIMENTAL

Evaporations were carried out under reduced pressure. ^{1}H N.m.r. spectra were measured on a Perkin-Elmer R10 spectrometer at 60 MHz. Unless otherwise stated deuteriochloroform was used as solvent with tetramethylsilane as internal standard; with [$^2H_6$]dimethyl sulphoxide as solvent, sodium 3-trimethylsilylpropane-1-sulphonate was used. U.v. spectra were recorded on a Perkin-Elmer 137 spectrophotometer with ethanol as solvent.

3-*Chloro*[1,4]*benzodioxino*[2,3-c]*pyridazine* (II; R^1 = Cl, R^2 = H).—(*a*) Catechol (18 g, 0·164 mol) was added to sodium hydride (50% dispersion; 16 g, 0·33 mol) in dry 1,2-dimethoxyethane (200 ml). The suspension was stirred for 30 min, treated with 3,4,6-trichloropyridazine (30 g, 0·164 mol) in dimethoxyethane (50 ml), and then stirred under reflux (bath at 85°) for 2 h. Most of the solvent was evaporated off and water (200 ml) was added. Filtration and crystallisations from butan-2-one gave the *product* (17·0 g, 47%), m.p. 169—170° (Found: C, 54·1; H, 2·3; N, 12·6. $C_{10}H_5ClN_2O_2$ requires C, 54·4; H, 2·3; N, 12·7%), $\lambda_{max.}$ 314 nm (log ε 3·68), τ 2·9—3·0 (4H, m, ArH) and 3·05 (1H, s, H-4).

The following compounds were prepared similarly: (i) from 3,4,5-trichloropyridazine, 1-*chloro*[1,4]*benzodioxino*-[2,3-d]*pyridazine* (III; R = Cl) (48%), m.p. 198—200° (from chloroform or diethyl ketone) (Found: C, 54·1; H, 2·4; N, 12·6%), $\lambda_{max.}$ 287 nm (log ε 3·25), τ 2·9—3·1 (4H, m, ArH) and 1·3 (1H, s, H-1); (ii) from 4-nitrocatechol and 3,4,6-trichloropyridazine, 3-*chloro*-6-*nitro*[1,4]*benzodioxino*-[2,3-c]*pyridazine* (36%), m.p. 281—283° (from diethyl ketone) (Found: C, 45·1; H, 1·5; N, 15·7. $C_{10}H_4ClN_3O_4$ requires C, 45·3; H, 1·5; N, 15·8%), $\lambda_{max.}$ 294 nm (log ε 3·94), τ 2·35 (1H, s, H-4) [superimposed on 1·9—2·7 (3H, m, ArH)]; and (iii) from 3-methoxycatechol and 3,4,6-trichloropyridazine, 3-*chloro*-5-*methoxy*[1,4]*benzodioxino*[2,3-c]*pyridazine* (44%), m.p. 176—178° (from ether) (Found: C, 52·6; H, 2·7; N, 11·1. $C_{11}H_7ClN_2O_3$ requires C, 52·7; H, 2·8; N, 11·2%), $\lambda_{max.}$ 289 and 317 nm (log ε 3·78 and 3·74), τ 2·7—3·6 (3H, m, ArH), 3·0 (1H, s, H-4), and 6·1 (3H, s, OMe).

(*b*) 3,4,6-Trichloropyridazine (60 g) in diethyl ketone (250 ml) was added to catechol (36 g) and anhydrous potassium carbonate (60 g) in the same solvent (250 ml). The mixture was stirred under reflux (bath at 120°) for 4 h and filtered hot. The chloro-compound (38·2 g, 53%), which separated on cooling the filtrate, had m.p. 167—169°.

[1,4]*Benzodioxino*[2,3-c]*pyridazine* (II; R^1 = R^2 = H).—3-Chloro[1,4]benzodioxino[2,3-*c*]pyridazine (0·5 g) in ethyl acetate (25 ml) containing triethylamine (2 ml) was hydrogenated over palladised charcoal (0·5 g; 5%). The filtered solution was washed with water and evaporated to give the product (0·4 g). A sample of the *base*, purified by sublimation at 100° and 25 mmHg, had m.p. 137—138° (Found: C, 64·4; H, 3·5; N, 15·0. $C_{10}H_6N_2O_2$ required C, 64·5; H, 3·3; N, 15·1%), $\lambda_{max.}$ 305 nm (log ε 3·28), τ 2·9—3·2 (4H, m, ArH), 1·28 (1H, d, *J* 9 Hz, H-3, part of ABq), and 3·08 (1H, d, *J* 9 Hz, H-4, part of ABq superimposed on aromatic multiplet).

Similar reduction of 1-chloro[1,4]benzodioxino[2,3-*d*]-pyridazine gave [1,4]*benzodioxino*[2,3-d]*pyridazine* (III; R=H) (71%), m.p. 197—198° (from diethyl ketone) (Found: C, 64·4; H, 3·3; N, 15·2%), $\lambda_{max.}$ 288 nm (log ε 3·30), τ 1·3 (2H, s, H-1 and -4) and 3·1 (4H, m, ArH).

Reactions of 3-*Chloro*[1,4]*benzodioxino*[2,3-c]*pyridazine with Alkoxides.*—(i) *Sodium methoxide at* 65°. A solution of sodium methoxide [from sodium (0·9 g)] in dry methanol (50 ml) was treated with the chloro-compound (1·0 g) and boiled under reflux for 16 h. Addition of 2N-sodium hydroxide (10 ml) to the cooled solution gave a precipitate, which was collected and crystallised from hexane. 6-*Chloro*-3,4-*dimethoxypyridazine* (0·3 g, 38%) had m.p. 127—128° (Found: C, 41·7; H, 4·2; N, 15·6. $C_6H_7ClN_2O_2$ requires C, 41·3; H, 4·0; N, 16·1%), $\lambda_{max.}$ 276 nm (log ε 3·37), τ 3·26 (1H, s, H-5), 5·86 (3H, s, 3-OMe), and 6·08 (3H, s, 4-OMe).

(ii) *Sodium methoxide at* −70°. The chloro-compound (2 g) in methanol (50 ml) was added dropwise to a stirred solution of sodium methoxide [from sodium (0·25 g)] in methanol (25 ml) cooled in acetone–solid carbon dioxide. A white precipitate soon formed and the suspension was cooled and stirred for 6 h. The temperature was allowed to rise to −30° and 2N-hydrochloric acid was added dropwise to neutralise the mixture. Evaporation gave a solid which was dissolved in chloroform; the solution was washed with water and evaporated. Crystallisations from diethyl ketone gave 3-*chloro*-6-(2-*hydroxyphenoxy*)-5-*methoxypyridazine* (0·5 g), m.p. 196—197° (Found: C, 52·6; H, 3·9; N, 10·6. $C_{11}H_9ClN_2O_3$ requires C, 52·3; H, 3·6; N, 11·1%); $\lambda_{max.}$ 276 nm (log ε 3·54); τ 2·80 (1H, s, H-5), 2·98 (4H, m, ArH), and 6·00 (3H, s, OMe).

(iii) *Potassium benzyl oxide.* Potassium benzyl oxide (3·1 g) was added to the chloro-compound (4·4 g) in xylene (100 ml) and the mixture was boiled under reflux (bath at 160°) for 1·5 h. The cooled solution was filtered through a short column of alumina and evaporated. The residue was extracted with benzene and applied to a column of silica gel (500 g). Elution with benzene and crystallisation from

hexane yielded 3,4-*bisbenzyloxy*-6-*chloropyridazine* (1·6 g), m.p. 106° (resolidifying and remelting at 126—127°) (Found: C, 66·7; H, 4·7; N, 8·6. $C_{18}H_{15}ClN_2O_2$ requires C, 66·2; H, 4·6; N, 8·6%), $\lambda_{max.}$ 277 nm (log ε 3·39), τ 2·60 (10H, m, ArH), 3·20 (1H, s, H-5), 4·09 (2H, s, CH_2Ph), and 4·29 (2H, s, CH_2Ph).

Elution of the column with ether then gave 2-*benzyl*-4-*benzyloxy*-6-*chloropyridazin*-3(2H)-*one* (1·0 g), m.p. 128—129° (from hexane–carbon tetrachloride) (Found: C, 66·1; H, 4·6; N, 8·5%), $\lambda_{max.}$ 279 nm (log ε 3·24), τ 2·6 (10H, m, ArH), 3·20 (1H, s, H-5), 4·39 (2H, s, O·CH_2Ph), and 4·82 (2H, s, N·CH_2Ph).

When 3,4-bisbenzyloxy-6-chloropyridazine was heated at 110°, it gave the rearrangement product, m.p. 128—129° (mixed m.p.; identical i.r. solution spectra).

6-*Chloropyridazine*-3,4-*diol*.— 3,4-Bisbenzyloxy-6-chloropyridazine (0·5 g) in ethyl acetate (50 ml) was hydrogenated over palladised charcoal (0·5 g; 5%). Evaporation of the filtered solution and crystallisations from hexane–ethyl acetate gave 6-*chloropyridazine*-3,4-*diol* (0·15 g), m.p. 111—112° (Found: C, 33·5; H, 2·1; N, 19·5. $C_4H_3ClN_2O_2$ requires C, 32·8; H, 2·1; N, 19·1%), $\lambda_{max.}$ 289 nm (log ε 3·72), $\nu_{max.}$ 1640 cm^{-1} (C=O), τ [$(CD_3)_2SO$] 2·60 (s, H-5).

[1,4]*Benzodioxino*[2,3-c]*pyridazin*-3(2H)-*one* (VI).—A solution of 3-chloro[1,4]benzodioxino[2,3-*c*]pyridazine (1·0 g) in dry, redistilled n-hexanol (20 ml) was boiled under reflux (bath at 170°) for 26 h and then evaporated. The residue was washed with ether and crystallised from ethanol to give the *pyridazinone* (0·28 g), m.p. 295—296° (Found: C, 59·2; H, 3·0; N, 13·8. $C_{10}H_6N_2O_3$ requires C, 59·4; H, 3·0; N, 13·9%), $\lambda_{max.}$ 287 nm (log ε 3·78), τ 2·9 (4H, m, ArH) and 3·56 (1H, s, H-4).

Reaction of 3-*Chloro*[1,4]*benzodioxino*[2,3-c]*pyridazine with Amines*.—The chloro-compound (5 g) and anhydrous diethylamine (40 ml) were heated at 170° in a sealed tube for 14 h. The cooled mixture was poured into sodium hydrogen carbonate solution. Isolation with ethyl acetate gave a dark oil which was dissolved in benzene and passed through a short column of alumina, which was eluted with benzene. Evaporation, trituration with ether, filtration, and crystallisations from hexane gave 3-*diethylamino*[1,4]*dibenzodioxino*[2,3-c]*pyridazine* (1·54 g), m.p. 118—119° (Found: C, 65·5; H, 6·1; N, 16·3. $C_{14}H_{15}N_3O_2$ requires C, 65·4; H, 5·9; N, 16·3%), $\lambda_{max.}$ 276 and 350 nm (log ε 4·08 and 3·131), τ 3·0 (4H, m, ArH), 3·7 (1H, s, H-4), 6·45 (4H, q, *J* 7 Hz, CH_2·CH_3), 8·8 (6H, t, *J* 7 Hz ·CH_2·CH_3).

The following compounds were prepared similarly by boiling with the amine under reflux for 3 h: 3-*benzyl*(*methyl*)*amino*[1,4]*benzodioxino*[2,3-c]*pyridazine* (51%), m.p. 150—151° (Found: C, 70·8; H, 4·9; N, 13·8. $C_{18}H_{15}N_3O_2$ requires C, 70·8; H, 5·0; N, 13·8%), $\lambda_{max.}$ 305 nm (log ε 3·28), τ 2·7 (5H, s, *Ph*CH_2), 2·95—3·15 (4H, m, $C_6H_4O_2$), 3·7 (1H, s, H-4), 5·25 (2H, s, CH_2Ph), and 6·85 (3H, s, NMe); and 3-(4-*methylpiperazin*-1-*yl*)[1,4]*benzodioxino*[2,3-c]*pyridazine* (36%), m.p. 169—170° (Found: C, 63·3; H, 5·8; N, 19·9. $C_{15}H_{16}N_4O_2$ requires C, 63·4; H, 5·7; N, 19·7%), τ 3·0 (4H, m, ArH), 3·5 (1H, s, H-4), 6·3—6·6 (4H, part of A_2X_2m, CH_2·N·CH_2), 7·3—7·6 (4H, part of A_2X_2m, CH_2·NMe·CH_2), and 7·65 (3H, s, NMe).

The chloro-compound (2·5 g) was boiled with pyrrolidine (15 ml) under reflux for 3 h. The oil obtained by evaporation was dissolved in chloroform and washed with sodium hydrogen carbonate solution and water. Evaporation of the dried ($MgSO_4$) solution left a solid which was crystallised from chloroform–hexane to give 6-*chloro*-3-(2-*hydroxyphenoxy*)-4-(*pyrrolidin*-1-*yl*)*pyridazine* (1·3 g), m.p. 170—172° (Found: C, 57·6; H, 4·8; N, 14·4. $C_{14}H_{14}ClN_3O_2$ requires C, 57·6; H, 4·8; N, 14·4%), $\lambda_{max.}$ 296 and 337 nm (log ε 3·66 and 3·18), τ [$CDCl_3$–$(CD_3)_2SO$] 3·0 (4H, m, ArH), 3·6 (1H, s, H-5), 6·3 (4H, m, CH_2·N·CH_2), 6·7 (1H, s, OH), and 8·0 (4H, m, 3- and 4-CH_2).

Similarly piperidine gave 6-*chloro*-3-(2-*hydroxyphenoxy*)-4-*piperidinopyridazine* (26%), m.p. 151—151·5° (from benzene) (Found: C, 58·3; H, 5·3; N, 13·4. $C_{15}H_{16}ClN_3O_2$ requires C, 58·9; H, 5·3; N, 13·7%), $\lambda_{max.}$ 286 and 334 nm (log ε 3·88 and 3·43), τ 2·9 (4H, m, ArH), 3·2 (1H, s, H-5), 6·5br (4H, s, CH_2·N·CH_2), and 8·2br (6H, s, $[CH_2]_3$).

Under the same conditions, morpholine gave 3-*morpholino*[1,4]*benzodioxino*[2,3-c]*pyridazine* (44%), m.p. 252—254° (from chloroform–hexane) (Found: C, 61·7; H, 4·8; N, 15·6. $C_{14}H_{13}N_3O_3$ requires C, 62·0; H, 4·8; N, 15·5%), τ 3·0 (4H, m, ArH), 3·6 (1H, s, H-4), 6·0—6·3 (4H, A_2X_2m, CH_2·O·CH_2), and 6·3—6·6 (4H, A_2X_2m, CH_2·N·CH_2).

The chloro-compound (5 g) and morpholine (20 ml) were heated at 170° for 14 h in an autoclave. Evaporation gave an oil which was dissolved in benzene, washed with sodium hydrogen carbonate solution, and passed through a short column of alumina. Concentration and crystallisations from benzene gave 3,4,6-trimorpholinopyridazine (4·4 g), m.p. 201—202° (Found: C, 57·6; H, 7·8; N, 20·6. Calc. for $C_{16}H_{25}N_5O_3$: C, 57·3; H, 7·5; N, 20·9%) (lit.,[7] m.p. 199—201°).

3-(2-*Hydroxyphenoxy*)-4-*methoxypyridazine*.— [1,4]Benzodioxino[2,3-*c*]pyridazine (2 g) was added to a solution of sodium methoxide (2 g) in methanol (25 ml) and heated under reflux for 4 h. Evaporation, addition of water, and isolation with chloroform gave the *phenol* (36%), m.p. 178—180° (from acetone–hexane) (Found: C, 60·4; H, 4·6; N, 13·0. $C_{11}H_{10}N_2O_3$ requires C, 60·5; H, 4·6; N, 12·8%), τ 1·32 (1H, half of ABq, *J* 5 Hz, H-6), 3·04 (1H, half of ABq, *J* 5 Hz, H-5), 2·87 (4H, m, ArH), and 6·03 (3H, s, OMe).

Quaternisation of [1,4]*Benzodioxino*[2,3-c]*pyridazine*.— The base (1·0 g) in methylene chloride (25 ml) was treated with triethyloxonium fluoroborate (1 g) in methylene chloride (10 ml). The solution was boiled under reflux for 1 h, concentrated to small volume, and filtered. After washing with ether, the solid was crystallised from ethanol to give the salt, probably 2-*ethyl*[1,4]*benzodioxino*[2,3-c]*pyridazinium fluoroborate* as the *ethanolate* (1·8 g), m.p. 134—135° (Found: C, 48·1; H, 4·7; N, 8·0. $C_{14}H_{17}BF_4N_2O_3$ requires C, 48·3; H, 4·9; N, 8·0%), $\lambda_{max.}$ 276 nm (log ε 3·93), τ [$(CD_3)_2SO$] 0·7 (1H, H-3) and 2·1 (1H, H-4) (ABq, J_o 6 Hz), 2·8 (4H, m, ArH), 5·6 (2H, q, *J* 7 Hz, N·CH_2·CH_3), 6·2 (2H, q, *J* 7 Hz, HO·CH_2·CH_3), 8·6 (3H, t *J* 7 Hz, N·CH_2·CH_3), and 8·7 (3H, t, *J* 7 Hz, HO·CH_2·CH_3).

1-(4-*Methylpiperazin*-1-*yl*)[1,4]*benzodioxino*[2,3-d]*pyridazine*.—A solution of 1-chloro[1,4]benzodioxino[2,3-d]-pyridazine (4·0 g) in *N*-methylpiperazine was boiled under reflux for 3 h. Evaporation, trituration with water, and crystallisation from benzene gave the *base* (3·2 g), m.p. 171—172° (Found: C, 63·8; H, 5·8; N, 19·5. $C_{15}H_{16}N_4O_2$ requires C, 63·4; H, 5·7; N, 19·7%), $\lambda_{max.}$ 282 nm (log ε 3·71), τ 1·6 (1H, s, H-4), 3·05 (4H, m, ArH), 6·3—6·6 (4H, part of A_2X_2m, CH_2·N·CH_2), 7·3—7·6 (4H, part of A_2X_2m, CH_2·NMe·CH_2), and 7·65 (3H, s, NMe).

Quaternisation of 1-*Chloro*[1,4]*benzodioxino*[2,3-d]*pyridazine*.—The base (1 g) in methylene chloride (25 ml) was added to triethyloxonium fluoroborate (1 g) in methylene chloride (20 ml). The solution was boiled under reflux for 1 h and evaporated, and the residue was crystallised from

ethanol to give the salt, probably *1-chloro-3-ethyl*[1,4]*benzodioxino*[2,3-d]*pyridazinium fluoroborate* (1·5 g), which decomposed without melting (Found: C, 42·2; H, 3·0; N, 8·3. $C_{12}H_{10}BClF_4N_2O_2$ requires C, 42·8; H, 3·0; N, 8·3%), $\lambda_{max.}$ 288 nm (log ε 3·80), τ 0·25 (1H, s, H-1), 2·9 (4H, m, ArH), 5·45 (2H, q, *J* 7 Hz, CH_2·CH_3), and 8·5 (3H, t, *J* 7 Hz. CH_2·CH_3).

[1,4]*Benzodioxino*[2,3-b]*quinoxaline* (with J. A. Groves).—(*a*) 2,3-Dichloroquinoxaline (10 g) in 1,2-dimethoxyethane (100 ml) was added to a suspension of the disodium salt of catechol [from catechol (5·6 g) and sodium hydride (50%; 4·8 g)] in the same solvent (100 ml). The mixture was stirred and heated under reflux for 2 h, cooled, and filtered. The filtrate was decolourised (charcoal) and evaporated; crystallisations from ethanol gave the product (4·6 g, 40%), m.p. 264—265° (lit.,[5] 264—265°).

(*b*) A solution of 2,3-dichloroquinoxaline and catechol (11·2 g) in diethyl ketone (75 ml) was stirred and boiled under reflux with potassium carbonate (26 g) for 8 h. The hot solution was filtered and, on cooling, the product separated; m.p. 265—266° (from ethanol) (yield 20·4 g, 86%).

[14] G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 1948, 519, 622.

Reaction of [1,4]*Benzodioxino*[2,3-b]*quinoxaline with Sodium Alkoxides* (with J. A. Groves).—(*a*) The base (1 g) was added to sodium methoxide (0·6 g) in methanol (50 ml) and the solution was boiled under reflux for 2 h. Neutralisation with 2N-hydrochloric acid precipitated 2,3-dimethoxyquinoxaline (0·8 g), m.p. and mixed m.p. 90—92° (from methanol) (lit.,[14] 85°). Similarly with ethanolic sodium ethoxide, the base gave 2,3-diethoxyquinoxaline (47%), m.p. 72—74° (lit.,[15] m.p. 77—78°).

(*b*) Sodium (28 mg, 1·2 mg atom) was dissolved in absolute ethanol (50 ml) and the base (0·5 g, 2·1 mmol) was added. The solution was boiled under reflux for 3 h and then evaporated. Addition of water, filtration, and recrystallisations from ethanol gave *2-ethoxy-3-(2-hydroxyphenoxy)-quinoxaline* (50 mg), m.p. 143—144° (Found: C, 68·0; H, 5·1; N, 9·9. $C_{16}H_{14}N_2O_3$ requires C, 68·1; H, 5·0; N, 9·9%), $\nu_{max.}$ 3550 cm^{-1} (OH).

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