Halogeno-*o*-phenylenediamines and Derived Heterocycles. Part I. Reductive Fission of Benzotriazoles to *o*-Phenylenediamines

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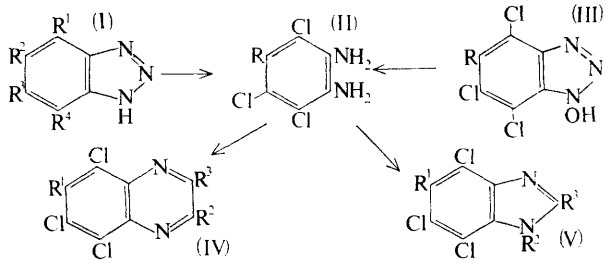
4,5,6,7-Tetrachlorobenzotriazole and its 1-hydroxy-derivative have been reduced with zinc and hydrochloric acid to give 3,4,5,6-tetrachloro-*o*-phenylenediamine (II; R = Cl) in good yield. The corresponding diamines (II; R = Me or F) were obtained similarly from 4,5,7-trichloro-6-methyl(or fluoro)benzotriazole. Alternative syntheses of the tetrachloro- and methyltrichloro-phenylenediamines are described. Benzimidazoles, quinoxalines, and other heterocycles derived from the diamines, especially from tetrachloro-*o*-phenylenediamine, are reported.

In the course of our work, we required 4,5,6,7-tetrachlorobenzotriazole (I; $R^1 = R^2 = R^3 = R^4 = Cl$), a known compound obtained by treating benzotriazole with boiling *aqua regia*.[1] Although the reaction conditions appear drastic, 4,5,6,7-tetrachlorobenzotriazole is obtained in high yield, and indeed the use of *aqua regia* for the complete chlorination of mono-substituted benzotriazoles [2,3] has been extended. The biological activity of 4,5,6,7-tetrachlorobenzotriazole led us to consider syntheses of other polychloro-heterocycles.

Benzotriazole can be reduced by sodium in liquid ammonia [4] to *o*-phenylenediamine, and *N*-substituted benzotriazoles can be reduced with sodium in butanol [5] or with zinc [6] to give *N*-substituted *o*-phenylenediamines. As 3,4,5,6-tetrachloro-*o*-phenylenediamine (II; R = Cl) is a key intermediate in the preparation of tetrachlorobenzo-heterocycles, the reductive ring cleavage of 4,5,6,7-tetrachlorobenzotriazole was investigated; reaction with zinc and hydrochloric acid conveniently gave this diamine in good yield. The diamine, not previously described, could be cyclised to a wide variety of previously unobtainable tetrachloro-heterocyclic derivatives.



This simple synthetic route to *o*-phenylenediamines was applied to certain other polyhalogeno-benzotriazoles; the diamines were then cyclised by the usual methods to give the corresponding benzo-heterocycles.

Thus, 5-fluorobenzotriazole [7] was obtained from the 5-amino-compound (I; $R^1 = R^3 = R^4 = H$, $R^2 = NH_2$) by the Schiemann reaction and was chlorinated with *aqua regia* to yield 4,5,7-trichloro-6-fluorobenzotriazole. Reduction of the latter with zinc and hydrochloric acid gave a high yield of 3,4,6-trichloro-5-fluoro-*o*-phenylenediamine (II; R = F), which on treatment with glyoxal gave the corresponding quinoxaline (IV; $R^1 = F$, $R^2 = R^3 = H$). Trifluoroacetic acid and the diamine gave the 2-trifluoromethylbenzimidazole (V; $R^1 = F$, $R^2 = H$, $R^3 = CF_3$). 2,5,6-Trichlorotoluene-3,4-diamine (II; R = Me) was similarly obtained from 4,5,7-trichloro-6-methylbenzotriazole,[2] and recyclised to give the benzimidazole (V; $R^1 = Me$, $R^2 = H$, $R^3 = CF_3$) and the quinoxaline (IV; $R^1 = Me$, $R^2 = R^3 = H$).

Although tetrachloro-*o*-phenylenediamine (II; R = Cl) was successfully obtained by this route (65%), 4,5,6,7-tetrabromobenzotriazole [3] (I; $R^1 = R^2 = R^3 = R^4 = Br$) did not yield the tetrabromo-*o*-phenylenediamine. No product was identified, but it is known that zinc dust will readily debrominate heterocyclic systems in acid media.[8]

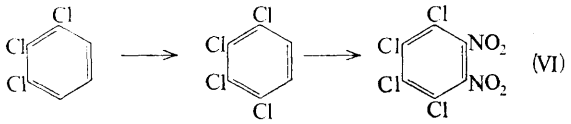
4,5,6,7-Tetrachloro-1-hydroxybenzotriazole (III; R = Cl), prepared by the action of hydrazine on pentachloronitrobenzene, could also be reduced directly to the *o*-phenylenediamine (II; R = Cl) (81%) with zinc and hydrochloric acid. This method of converting *o*-chloronitrobenzenes into *o*-phenylenediamines is limited however, since in certain cases the phenylhydrazine results from the replacement of the nitro-group [9] with hydrazine.

The zinc–acid reduction method is not applicable to nitrobenzotriazoles. However, nitro-*o*-phenylenediamines can be obtained by selective reduction of the benzofuroxan and benzo-2,1,3-selenadiazole systems with hydriodic acid; [10,11] these may then be recyclised to the required nitro-halogeno-heterocycles. It is also possible to introduce a nitro-group directly into the polychloro-heterocycles by conventional substitution methods.[12]

It was found later [13] that the following route was convenient for the large scale preparation of 3,4,5,6-tetrachloro-*o*-phenylenediamine. 1,2,3-Trichlorobenzene was

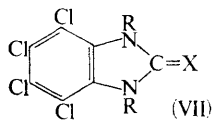
[1] R. H. Wiley, K. F. Hussung, and J. Moffat, *J. Amer. Chem. Soc.*, 1955, **77**, 5105.
[2] T. Zincke and R. Arzberger, *Annalen*, 1888, **249**, 370.
[3] R. H. Wiley and K. F. Hussung, *J. Amer. Chem. Soc.*, 1957, **79**, 4395.
[4] N. O. Cappel and W. C. Fernelius, *J. Org. Chem.*, 1940, **5**, 40.
[5] H. Stetter, *Chem. Ber.*, 1953, **86**, 69.
[6] M. Wakae, K. Konishi, M. Furukawa, and E. Hamada (*Chem. Abs.*, 1964, **61**, 3096b); *Osaka Furitsu Kogyo-Shoreikan Hokoku*, 1962, No. **27**, 46.
[7] I. Tamm, R. Bablanian, M. M. Nemes, C. H. Shunk, F. M. Robinson, and K. A. Folkers, *J. Exp. Medicine*, 1961, **113**, 625.
[8] W. Baczynski and S. Niementowski, *Bull. Acad. Sci. Cracow*, 1902, 421.
[9] M. B. Purdew, personal communication.
[10] J. H. Boyer and W. Schoen, *J. Amer. Chem. Soc.*, 1956, **78**, 423.
[11] J. A. Elvidge, G. T. Newbold, A. Percival, and I. R. Senciall, *J. Chem. Soc.*, 1965, 5119.
[12] G. T. Newbold, P. J. Brooker, and M. B. Purdew, to be published.
[13] J. F. Harris and D. W. J. Lane, U.S.P. 3,166,594/1965.

first chlorinated to give 1,2,3,4-tetrachlorobenzene, which was then dinitrated to yield 1,2,3,4-tetrachloro-5,6-dinitrobenzene (VI). The dinitro-compound was then reduced with stannous chloride–hydrochloric acid, or iron–hydrochloric acid, to give the required *o*-phenylenediamine.

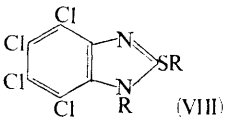


(VI)

Several benzimidazoles (see Table 1) were derived from 3,4,5,6-tetrachloro-*o*-phenylenediamine (II; R = Cl); reaction of the latter with formic acid afforded the reported [14] 4,5,6,7-tetrachlorobenzimidazole (V; R^1 = Cl, R^2 = R^3 = H), for which a preparative method has not hitherto been published. Reaction with trifluoroacetic acid gave the corresponding 2-trifluoromethyl compound (V; R^1 = Cl, R^2 = H, R^2 = CF_3), the preparation of which, by complete chlorination of 2-trifluoromethylbenzimidazole, has recently been described.[15,16] Compound (V) (R^1 = Cl, R^2 = R^3 = H) was characterised by the preparation of its 1-methyl, 1-n-butyl, and 1-trichloromethylthio-derivatives. Anhydrides were preferred for the preparation of the 2-methyl, 2-n-propyl, 2-n-amyl and 2-(2-carboxyethyl) derivatives of 4,5,6,7-tetrachlorobenzimidazole from this diamine. 4,5,6,7-Tetrachloro-2-(*p*-nitrophenyl)benzimidazole was conveniently prepared by reaction of (II; R = Cl) with *p*-nitrobenzaldehyde, followed by oxidation of the intermediate Schiff base with lead tetraacetate. 4,5,6,7-Tetrachloro-2-benzimidazolinone (VII; R = H, X = O), was formed by reaction of the diamine (II; R = Cl) with urea. Cyclisation of the tetrachloro-*o*-phenylenediamine with thiophosgene, or better, carbon disulphide in dimethylformamide,[17] afforded 4,5,6,7-tetrachlorobenzimidazoline-2-thione (VII; R = H, X = S), which on alkylation with n-butyl iodide or prop-2-ynyl bromide gave the disubstituted derivatives (VIII; R = Bu- and CH_2·C:CH).



(VII)



(VIII)

This substitution pattern was confirmed by the ^{1}H n.m.r. spectra. The di-n-butyl derivative in deuteriochloroform showed triplets at τ 5·63 and 6·56 (*J* 7 c./sec.) for N–CH_2 and S–CH_2 respectively, together with methylene signals from τ 7·95 to 8·85, and distorted triplets at τ *ca.* 9·03 for the terminal methyl groups.

The diprop-2-ynyl compound in pyridine gave doublets at τ 4·66 and 5·49 and triplets at τ 6·40 and 6·71 from the acetylenic protons, both with *J* 2·7 c./sec. Again, the down-field lines are assigned to the *N*-substituent.

Several *N*-substituted derivatives of the diamine (II; R = Cl) were also prepared. Reaction with acetic anhydride (1 mol.) at room temperature gave the monoacetyl derivative (IX; R^1 = H, R^2 = Ac), and reaction with toluene-*p*-sulphonyl chloride (2 mol.) in pyridine at 60° yielded the *NN'*-ditosyl derivative (IX; R^1 = R^2 = *p*-MeC_6H_4·SO_2). Unexpectedly, reaction with acetylacetone gave 4-(2-amino-3,4,5,6-tetrachloroanilino)pent-3-ene-2-one (IX; R^1 = H, R^2 = CMe:CHAc). This structure was assigned on the basis of ^{1}H n.m.r. data. For a solution in deuteriochloroform, methyl signals were observed at τ 8·28 and 7·89, together with one olefinic proton signal at τ 4·68, and broad signals, centres, τ 5·34 (2H) and −1·64 ascribed to the three

TABLE 1

Preparation and properties of 4,5,6,7-tetrachloro-benzimidazoles (V; R^1 = Cl)

Compound		Yield	Solvent		Found (%)				Required (%)		
R^2	R^3	(%)	for cryst.	M. p.	C	H	N	Formula	C	H	N
H	H [a]	95 [b]	HOAc	327—328°	32·8	1·0	11·1	$C_7HCl_4N_2$	32·8	0·8	10·9
H	CF_3 [c]	50 [b]	C_6H_6	285	30·9	0·8	8·6	$C_8HCl_4F_3N_2$	29·7	0·3	8·7
H	Me [d]	86 [e]	Xylene	345—350 *	35·8	1·7	10·5	$C_8H_4Cl_4N_2$	35·6	1·5	10·4
H	Pr^n	66 [e]	MeOH	288—290	40·8	3·0	8·9	$C_{10}H_8Cl_4N_2$	40·3	2·7	9·4
H	n-C_5H_{11}	75 [e]	Dioxan	293—295	43·8	3·9	8·5	$C_{12}H_{12}Cl_4N_2$	44·2	3·7	8·6
H	CH_2·CH_2·CO_2H	54 [f]	aq.HOAc	273—274	36·4	1·9	8·7	$C_{10}H_6Cl_4N_2O_2$	36·6	1·8	8·5
H	OH † [g]	84 [h]		>360	31·0	1·0	10·3	$C_7H_2Cl_4N_2O$	30·9	0·7	10·4
H	SH †	73 [h]	DMF	>360	29·0	0·8	9·5	$C_7H_2Cl_4N_2S$	29·2	0·8	9·8
H	*p*-$NO_2C_6H_4$	87 [h]	*h*	323—325	41·3	1·5	11·1	$C_{13}H_5Cl_4N_3O_2$	41·4	1·3	11·2
Me	H	40 [i]	C_6H_6	258—261	35·7	2·0	10·0	$C_8H_4Cl_4N_2$	35·6	1·5	10·4
Bu^n	H	82 [i]	MeOH	114	42·5	3·4	8·9	$C_{11}H_{10}Cl_4N_2$	42·3	3·2	9·0
$SCCl_3$	H	39 [h]	EtOAc	182—184	23·8	0·4	7·0	$C_8HCl_7N_2S$	23·7	0·3	6·9
Me	CF_3	52 [i]	EtOH	214—215	32·1	1·0	8·5	$C_9H_3Cl_4F_3N_2$	32·0	0·9	8·3
Bu^n	Bu^nS	75 [i]	EtOH	73—74	45·1	4·4	7·1	$C_{15}H_{18}Cl_4N_2S$	45·0	4·5	7·0
CH_2·C:CH	HC:C·CH_2S	30 [i]	$CHCl_3$ [j]	169—170	43·2	1·7	7·6	$C_{13}H_6Cl_4N_2S$	42·9	1·7	7·7

* Sulphate, m.p. 350° (decomp.) (see Experimental section). † Exists in tautomeric form.

[a] See ref. 14. [b] From the diamine with an excess of the appropriate acid under reflux. [c] See refs. 15 and 16. [d] See ref. 23. By use of an excess of the anhydride alone, or [f] in dioxan. [g] See ref. 24. [h] See Experimental section. [i] By alkylation of the appropriate benzimidazole. [j] After chromatography in benzene.

[14] I. Tamm, K. Folkers, and C. H. Shunk, *J. Bacteriol.*, 1956, **72**, 54.

[15] Shell Internationale Research Maatschappij, Neth. P. 6,410,413/1965.

[16] G. M. Fara and K. W. Cochran, *Boll. Ist. Sieroterap. Milan*, 1963, **42**, 630.

[17] R. W. Balsiger, A. L. Fikes, T. P. Johnston, and J. A. Montgomery, *J. Org. Chem.*, 1961, **26**, 3386.

amino-protons, one of which (lowest-field signal) was chelated to the side-chain carbonyl.

Treatment of an alcoholic solution of this last compound with sulphuric acid precipitated 4,5,6,7-tetrachloro-2-methylbenzimidazole (V; $R^1 = Cl$, $R^2 = H$, $R^3 = Me$) as its sulphate but cyclisation to give the corresponding 1,5-benzodiazepine was not achieved. However, reaction of the diamine (II; R = Cl) with acetoacetic ester in xylene solution gave the diazepinone (X; $R^1 = Cl$, $R^2 = H$). The parent of this system (X; $R^1 = R^2 = H$) and an isomeric product (XI) have been characterised by Davoll.[18] The above structure (X) for the tetrachloro-compound was confirmed by ^1H n.m.r. analysis, after methylation of the insoluble cyclic amide (X; $R^1 = Cl$, $R^2 = H$) with methyl iodide.

TABLE 2

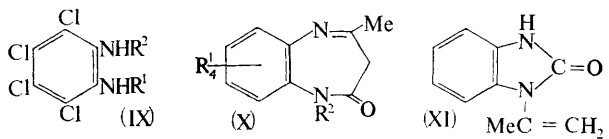
Preparation and properties of substituted 5,6,7,8- tetrachloroquinoxalines (IV; R = Cl)

Compound		Yield	Solvent		Found (%)				Required (%)		
R^2	R^3	(%)	for cryst.	M.p.	C	H	N	Formula	C	H	N
H	H	80 [a]	EtOAc	195—197°	35·7	0·8	10·5	$C_8H_2Cl_4N_2$	35·9	0·8	10·5
Me	H	55 [a]	EtOAc	174—175	38·5	1·6	10·1	$C_9H_4Cl_4N_2$	38·3	1·4	9·9
CCl_3	H	49 [b]	HOAc	186—187	28·3	0·3	7·5	$C_9HCl_7N_2$	28·1	0·3	7·3
Pr^n	H	50 [a]	EtOH	121—122	42·6	2·7	9·2	$C_{11}H_8Cl_4N_2$	42·6	2·6	9·0
Ph	H	49 [a]	Dioxan	276—278	48·7	1·9	8·3	$C_{14}H_6Cl_4N_2$	48·9	1·8	8·1
p-OHC_6H_4	H	66 [a]	[c]	313	47·0	1·7	7·7	$C_{14}H_6Cl_4N_2O$	46·7	1·7	7·8
OH	H *	95 [d]	$PhNO_2$	319	33·7	0·8	9·9	$C_8H_2Cl_4N_2O$	33·8	0·7	9·9
Cl	H	66 [e]	EtOAc	168—169	31·7	0·5	9·5	$C_8HCl_5N_2$	31·8	0·3	9·3
N_3	H	42 [f]	C_6H_6	170 (decomp.)	30·9	0·4	22·8	$C_8HCl_4N_5$	31·1	0·3	22·7
OMe	H	51 [f]	EtOAc	180—182	36·3	1·5	9·5	$C_9H_4Cl_4N_2O$	36·3	1·4	9·4
OEt	H	44 [f]	Dioxan	171—173	38·5	1·9	9·0	$C_{10}H_6Cl_4N_2O$	38·5	1·9	9·0
Me	Me	47 [a]	EtOAc	197—198	40·5	2·2	9·6	$C_{10}H_6Cl_4N_2$	40·6	2·0	9·5
Me	$CHCl_2$	45 [b]	HOAc	203—204	32·9	1·2	7·5	$C_{10}H_4Cl_6N_2$	32·9	1·1	7·7
$CHCl_2$	$CHCl_2$	82 [b]	HOAc	205—206	27·8	0·5	6·6	$C_{10}H_2Cl_8N_2$	27·7	0·5	6·5
Pr^n	Pr^n	50 [a]	EtOH	98—99	47·9	4·2	8·1	$C_{14}H_{14}Cl_4N_2$	47·8	4·0	8·0
Ph	Ph	88 [a,g]	C_6H_6	250—252	57·3	2·7	6·5	$C_{26}H_{10}Cl_4N_2$	57·2	2·4	6·7
OH	OH *	45 [h]	DMF	>360	32·3	0·7	9·3	$C_8H_2Cl_4N_2O_2$	32·0	0·7	9·3
OH	Me *	69 [h]	HOAc	324—325	36·1	1·5	9·7	$C_9H_3Cl_4N_2O$	36·3	1·4	9·4
OH	CO_2Et *	90 [h]	C_6H_6	244—245	37·4	1·8	7·7	$C_{11}H_6Cl_4N_2O_3$	37·1	1·7	7·9
Cl	Cl	21 [e]	HOAc	207—209	28·5		8·3	$C_8Cl_6N_2$	28·5		8·3

* Exists in tautomeric form.

[a] By condensation with appropriate 1,2-dicarbonyl compound in ethanol. [b] By chlorination of corresponding methyl compound. [c] 2-Ethoxyethanol. [d] By use of the α-keto-acid alone. [e] From hydroxy-compound by use of $POCl_3$–PCl_5. [f] From 2-chloro-compound with the appropriate nucleophile. [g] After prolonged heating (16 hr.). [h] By use of the ethyl α-keto-ester.

This derivative (X; $R^1 = Cl$, $R^2 = Me$) gave signals at τ 6·75 (NMe) and 7·55 (CMe) in deuteriochloroform solution, and the absence of any olefinic resonances clearly eliminated an *N*-isopropenylbenzimidazole structure.



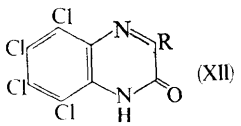
A slow inversion rate of the heterocyclic ring is indicated, since the methylene group in this ring gave rise to an AB quartet (τ 6·51 and 7·05, J 12, in deuteriochloroform; τ 5·67 and 6·19, J 12·5 c./sec., in trifluoroacetic acid solution). The *N*-methyl and *C*-methyl signals in trifluoroacetic acid were observed at τ 6·49 and 6·85 respectively; this large down-field shift indicated that protonation had taken place. The mass spectrum was also in agreement with the diazepinone structure (X; $R^1 = Cl$, $R^2 = Me$); the parent peak appeared at *m/e* 324, with associated isotopic chlorine signals appropriate to a tetrachloro-compound. The other peaks indicated that loss of CH_3 occurred first (*m/e* 309), and that the next most probable fragmentation was loss of NCO with rearrangement (*m/e* 282).

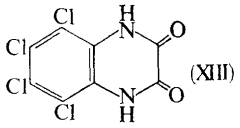
3,4,5,6-Tetrachloro-*o*-phenylenediamine (II; R = Cl) is also readily converted by reaction with 1,2-dicarbonyl compounds into quinoxaline derivatives (see Table 2); of these 5,6,7,8-tetrachloroquinoxaline and its 2-methyl analogue have been shown to be fungicides, particularly active against cucumber and apple mildews.[19] The chlorination of the 2-methyl and 2,3-dimethyl derivatives of 5,6,7,8-tetrachloroquinoxaline in acetic acid in the presence of sodium acetate has been studied; in the first case, the 2-trichloromethyl compound (IV; $R^1 = Cl$, $R^2 = H$, $R^3 = CCl_3$) is formed, whilst in the second, reaction at 70° with chlorine gives the 2-dichloromethyl-3-methyl compound (IV; $R^1 = Cl$, $R^2 = Me$, $R^3 = CHCl_2$). On irradiation, the 2,3-bisdichloromethyl derivative (IV; $R^1 = Cl$, $R^2 = R^3 = CHCl_2$) is formed; the structures were confirmed by ^1H n.m.r.

3,4,5,6-Tetrachloro-*o*-phenylenediamine reacts with glyoxylic acid to give 5,6,7,8-tetrachloroquinoxalin-2(1*H*)-one (XII; R = H), which with phosphorus pentachloride–phosphoryl chloride yields 2,5,6,7,8-pentachloroquinoxaline (IV; $R^1 = R^2 = Cl$, $R^3 = H$). The 2-chloro-substitutent can be replaced by a methoxy-, an ethoxy-, or an azido-group to give (IV; $R^1 = Cl$, $R^3 = H$, $R^2 = OMe$, OEt, or N_3). The tetrachloro-*o*-phenylylenediamine reacts with ethyl oxalate to give 5,6,7,8-tetrachloro-1,4-dihydroquinoxaline-2,3-dione (XIII) which can also be obtained by direct oxidation of 5,6,7,8-tetrachloroquinoxaline (IV; $R^1 = Cl$, $R^2 = R^3 = H$) with either nitric acid or hydrogen peroxide.

[18] J. Davoll, *J. Chem. Soc.*, 1960, 308.
[19] D. W. J. Lane and G. T. Newbold, B.P. 1,041,011/1966.

Vigorous treatment of (XIII) with phosphorus pentachloride–phosphoryl chloride affords 2,3,5,6,7,8-hexachloroquinoxaline (IV: $R^1 = R^2 = R^3 = Cl$).


(XII)


(XIII)

Reaction of tetrachloro-*o*-phenylenediamine with pyruvic acid gives 5,6,7,8-tetrachloro-3-methylquinoxalin-2(1*H*)-one (XII; R = Me), and with diethyl mesoxalate, 5,6,7,8-tetrachloro-3-ethoxycarbonylquinoxalin-2(1*H*)-one (XII; R = CO_2Et) is formed.

Further reactions and properties of heterocycles derived from halogeno-*o*-phenylenediamines will be the subject of additional communications in this series.

EXPERIMENTAL

I.r. spectra (KCl discs) were recorded with a Unicam SP 200 instrument. The ^1H n.mr. spectra were measured with a Perkin-Elmer R10 spectrometer at 60 Mc./sec. with tetramethylsilane as internal standard in deuteriochloroform solution except where otherwise stated.

3,4,5,6-*Tetrachloro*-o-*phenylenediamine* (II; R = Cl).—*Method* A. Concentrated hydrochloric acid (250 ml.) was added dropwise to a warm mixture of 4,5,6,7-tetrachlorobenzotriazole [1] (100 g.), zinc powder (100 g.), and ethanol (500 ml.). The mixture was then heated under reflux for 2 hr. and the hot supernatant was decanted from the inorganic residue and poured into a large volume of water. The precipitate was added to sodium hydroxide solution (10%; 500 ml.) and the mixture was extracted with ether. The extract was dried ($MgSO_4$) and evaporated to dryness, and the residue crystallised to give 3,4,5,6-*tetrachloro*-o-*phenylenediamine* (62 g., 65%), m.p. 234—235° (decomp.) (from aqueous ethanol) (Found: C, 29·3; H, 1·8; Cl, 58·0; N, 11·5. $C_6H_4Cl_4N_2$ requires C, 29·3; H, 1·7; Cl, 57·7; N, 11·4%).

4,5,6,7-Tetrachloro-1-hydroxybenzotriazole gave the tetrachloro-*o*-phenylene diamine (81%) by the same method.

Method B. 3,4,5,6-Tetrachloro-*o*-phenylenediamine was also obtained from 1,2,3-trichlorobenzene, in an overall yield of 77%.[13] Chlorination, dinitration, and finally stannous chloride reduction yielded the diamine, identical (m.p. and i.r. spectrum) with a sample prepared by method A.

5-*Fluorobenzotriazole*.[7]—5-Aminobenzotriazole hydrochloride [20] (36 g.) was suspended in 6N-hydrochloric acid (100 ml.) and cooled to 0°. A cold solution of sodium nitrite (14·8 g.) in water (20 ml.) was added slowly with stirring. The red solution was filtered through a ice-cold fine sinter funnel. A cold 40% solution of hydrofluoroboric acid (40·8 ml.) was added, in small amounts with vigorous stirring, to the clear filtrate. The mixture was then stirred for 45 mins. The fluoroborate derivative was filtered off and washed with small ice-cold portions of hydrofluoroboric acid, ethanol, and ether to give pink crystals (31·4 g., 47%), m.p. 158° (decomp.).

The dried fluoroborate (15 g.) was heated carefully at 22 mm. pressure, until decomposition commenced. Heating was stopped until the reaction had subsided, and then continued until all the fluoroborate had decomposed. The dark gum obtained was dissolved in sodium hydroxide solution (5%), the solution was filtered, and the filtrate acidified with hydrochloric acid. The precipitate was collected and washed with water, and the dried pink solid sublimed (135°/0·2 mm.) to give 5-*fluorobenzotriazole* (3·5 g., 51%), m.p. 148—149° (from benzene) (Found: C, 52·9; H, 3·1; N, 31·0. $C_6H_4FN_3$ requires C, 52·6; H, 3·0; N, 30·7%).

4,6,7-*Trichloro*-5-*fluorobenzotriazole*.—5-Fluorobenzotriazole (5·9 g.) was dissolved in hot acetic acid (107 ml.) and a mixture of concentrated hydrochloric acid (560 ml.) and concentrated nitric acid (187 ml.) was added. The solution was heated under reflux for 3 hr., cooled, and kept overnight at 0°. The precipitate was filtered off, washed thoroughly with water, and dried. Two crystallisations from aqueous acetic acid gave 4,6,7-*trichloro*-5-*fluorobenzotriazole* (6·6 g., 64%), m.p. 229—231° (Found: C, 30·2; H, 0·6; Cl, 44·0; N, 17·9. $C_6HCl_3FN_3$ requires C, 30·0; H, 0·4; Cl, 44·3; N, 17·5%).

3,4,6-*Trichloro*-5-*fluoro*-o-*phenylenediamine* (II; R = F).—This compound was prepared by the procedure for 3,4,5,6-tetrachloro-*o*-phenylenedimine. 4,6,7-Trichloro-5-fluorobenzotriazole (11·0 g.) gave 3,4,6-*trichloro*-5-*fluoro*-o-*phenylenediamine* (8·1 g., 76%), as needles, m.p. 165—167° (from ethanol) (Found: C, 31·6; H, 1·9; Cl, 46·6; N, 12·0. $C_6H_4Cl_3FN_2$ requires C, 31·4; H, 1·8; Cl, 46·4; N, 12·2%).

5,7,8-*Trichloro*-6-*fluoroquinoxaline*.—3,4,6-Trichloro-5-fluoro-*o*-phenylenediamine (7·65 g.) was dissolved in hot ethanol (72 ml.) and a solution of glyoxal (6·7 g.) in water (20 ml.) was added dropwise to the solution under reflux. The mixture was heated under reflux for 1 hr. and then kept overnight at 0°. The crystalline *product* was filtered off and washed with small amounts of ethanol and then water, to give 5,7,8-*trichloro*-6-*fluoroquinoxaline* (5·5 g., 66%), as pink needles, m.p. 155—157° [from ethanol (charcoal)] (Found: C, 38·3; H, 0·9; N, 11·1. $C_8H_2Cl_3FN_2$ requires C, 38·2; H, 0·8; N, 11·2%).

4,6,7-*Trichloro*-5-*fluoro*-2-*trifluoromethylbenzimidazole*.—A mixture of 3,4,6-trichloro-5-fluoro-*o*-phenylenediamine (12 g.) and trifluoroacetic acid (12 ml.) was heated at 95° for 16 hr., cooled, and poured into sodium hydroxide solution (10%; 90 ml.). The alkaline mixture was filtered and then acidified with concentrated hydrochloric acid. The precipitate was collected, washed with water, and crystallised to give 4,6,7-*trichloro*-5-*fluoro*-2-*trifluoromethylbenzimidazole* (13·6 g., 85%) as a pink solid, m.p. 246—248° [from aqueous ethanol (charcoal)] (Found: C, 31·5; H, 0·5; Cl, 34·4; N, 9·3. $C_8HCl_3F_4N_2$ requires C, 31·3; H, 0·4; Cl, 34·6; N, 9·1%).

4,6,7-*Trichloro*-5-*methylbenzotriazole*.[2]—5-Methylbenzotriazole [2] (21 g.) was dissolved in glacial acetic acid (400 ml.) and a mixture of concentrated hydrochloric acid (2,070 ml.) and concentrated nitric acid (690 ml.) was added. The mixture was refluxed for 3 hr. The solution was cooled and kept at 0° overnight; the crystals were then filtered off and washed thoroughly with water. Crystallisation from dilute acetic acid gave 4,6,7-trichloro-5-methylbenzotriazole (18·7 g., 50%), m.p. 252—253° (lit.,[2] 240°) (Found: C, 35·4; H, 1·8; Cl, 44·9; N, 17·9. Calc. for $C_7H_4Cl_3N_3$: C, 35·6; H, 1·7; Cl, 45·0; N, 17·8%).

2,5,6-*Trichlorotoluene*-3,4-*diamine* (II; R = Me).—*Method* A. This diamine was prepared (62%) from 4,6,7-trichloro-5-methylbenzotriazole (17·9 g.) by method A described above for the tetrachloro-analogue. The product (10·4 g.), m.p. 208—210° (from ethanol), was identical with the material obtained by the following method.

[20] T. Zincke, *Annalen*, 1900, **311**, 290.

Method B. 2,3,6-Trichlorotoluene (100 g.) was first dinitrated [21] to give 2,3,6-trichloro-4,5-dinitrotoluene (84·5 g., 58%) as needles, m.p. 141—143° (from ethanol) (lit., 143°). Reduction of this material (143 g.) with stannous chloride (800 g.) in concentrated hydrochloric acid (1 l.) containing ethanol (700 ml.), at reflux temperature, gave the diamine hydrochloride when the mixture was cooled after 1 hr. Basification and crystallisation of the solid yielded 2,5,6-trichlorotoluene-3,4-diamine (45 g., 40%), m.p. 212—214° (Found: C, 37·2; H, 3·2; N, 12·6. Calc. for $C_7H_7Cl_3N_2$: C, 37·3; H, 3·1; N, 12·4%). A m.p. of 200° has been reported for this compound.[22]

4,6,7-*Trichloro*-5-*methyl*-2-*trifluoromethylbenzimidazole*.—A mixture of 2,5,6-trichlorotoluene-3,4-diamine (12 g.) and trifluoroacetic acid (12 ml.) was heated at 100° for 16 hr. The product was isolated as described for the corresponding fluoro-2-trifluoromethylbenzimidazole. Sublimation of the crude product and crystallisation of the sublimate from toluene gave the required *product* (10·2 g., 62%), which sublimes above 165° (Found: C, 35·9; H, 1·5; N, 9·3. $C_9H_4Cl_3F_3N_2$ requires C, 35·6; H, 1·4; N, 9·3%).

4,6,7-*Trichloro*-5-*methylbenzimidazole*.— 2,5,6-Trichlorotoluene-3,4-diamine (15 g.) and formic acid (98%, 100 ml.) were heated together under reflux for 3 hr. The mixture was poured into sodium hydroxide solution (20%; 250 ml.) and the result was stirred thoroughly and filtered. The filtrate was acidified with concentrated hydrochloric acid, and the precipitate was collected and dried to give 4,6,7-*trichloro*-5-*methylbenzimidazole* (5 g., 31%) as needles, m.p. 323—326° (from ethanol) (Found: C, 40·7; H, 2·1; Cl, 45·4. $C_8H_5Cl_3N_2$ requires C, 40·8; H, 2·2; Cl, 45·2%).

N-*Substituted* o-*Phenylenediamines* (IX) *derived from* (II; R = Cl).—(i) The reported [23] monoacetyl derivative (R^1 = H, R^2 = Ac) was obtained from the tetrachloro-*o*-phenylenediamine (6·15 g., 1 mol.) by reaction with acetic anhydride (2·55 g., 1 mol.) in ethyl acetate (75 ml.). After 3 days at room temperature, the deposited solid was collected and purified to give the acetanilide (1·6 g., 23%), m.p. 227—228° (from xylene) (lit., 223—224°) (Found: C, 33·8; H, 2·3; N, 9·9. Calc. for $C_8H_6Cl_4N_2O$: C, 33·4; H, 2·1; N, 9·7%).

(ii) 4-(2-*Amino*-3,4,5,6-*tetrachloroanilino*)*pent*-3-*ene*-2-*one* (IX; R^1 = H, R^2 = CMe:CHAc).—Pentane-2,4-dione (20 g., 2 mol.) was added to a warm solution of the diamine (24·6 g., 1 mol.) in ethanol (250 ml.). After 12 hr., the deposited crystals were collected and the *product* (13·6 g., 42%) was obtained as needles, m.p. 175—176° (from carbon tetrachloride) (Found: C, 40·1; H, 3·1; N, 8·5. $C_{11}H_{10}Cl_4N_2O$ requires C, 40·3; H, 3·1; N, 8·5%), $\nu_{max.}$ (CCl_4) 3505 and 3420 (NH_2), 3200 (NH), 3000 (CH), 1635 (C=O), and 1280 (C–N) cm.$^{-1}$, τ ($CDCl_3$) 8·28 (3H, s, 5-Me), 7·89 (3H, s, 1-Me), 5·34br (2H, NH_2), 4·68 (1H, s, CH=C), and −1·64br (1H, NH).

Addition of concentrated sulphuric acid (2 mol.) to either the reaction mixture, or an ethanolic solution of the product, resulted in the rapid separation of 4,5,6,7-*tetrachloro*-2-*methylbenzimidazole sulphate*, m.p. 345—350° (decomp.) (Found: C, 26·1; H, 1·5; N, 7·8. $C_8H_4Cl_4N_2,H_2SO_4$ requires C, 26·2; H, 1·6; N, 7·7%).

(iii) 3,4,5,6-*Tetrachloro*-NN′-*bistoluene*-p-*sulphonyl*-o-*phenylenediamine* (IX; R^1 = R^2 = *p*-$MeC_6H_4SO_2$).—Reaction of the diamine (24·6 g., 1 mol.) with toluene-*p*-sulphonyl chloride (45 g., 2 mol.) in anhydrous pyridine (160 ml.) at 60°, gave the *ditosyl derivative* (36 g., 65%), m.p. 253—255°, as needles (from acetic acid) (Found: C, 43·3; H, 2·8; Cl, 25·3; N, 5·3. $C_{20}H_{16}Cl_4N_2S_2O_4$ requires C, 43·3; H, 2·9; Cl, 25·6; N, 5·1%).

Benzimidazoles (V; R^1 = Cl, R^2 = H).

(a) *General Procedure*.—The tetrachloro-*o*-phenylenediamine was heated at reflux temperature for 3 hr. with an excess of either 98% formic acid or the appropriate anhydride (see Table 1). When trifluoroacetic acid was used, the mixture was heated overnight on a steam-bath. The product, if crystalline, was filtered off when cold; otherwise the reaction mixture was poured into an excess of sodium hydroxide solution (10%), and the product liberated, after filtration, by acidification.

(b) *Other Compounds*.—4,5,6,7-*Tetrachloro*-2-(p-*nitrophenyl*)*benzimidazole*. An ethanolic solution of the tetrachloro-*o*-phenylenediamine (8·2 g.) was heated for a few minutes with *p*-nitrobenzaldehyde (5·7 g.); the anil, m.p. 190—192° was then collected. The orange-red solid (11·5 g.) was then dissolved in benzene and heated for 10 min. with lead tetra-acetate (12 g.). The deposited solid was collected and washed with benzene, and the *benzimidazole* (11 g., 87%) was obtained as pale yellow needles, m.p. 320—323° (from acetic acid). Recrystallisation from ethanol gave the pure compound, m.p. 323—325°.

4,5,6,7-*Tetrachlorobenzimidazolin*-2-*one*.[24] The diamine (24·6 g.) and an excess of urea (13 g.) were heated together until the initial melt resolidified. The product (21·6 g., 79%) was isolated by extraction with warm 2N-sodium hydroxide, followed by acidification and crystallisation from aqueous ethanol.

4,5,6,7-*Tetrachlorobenzimidazoline*-2-*thione*. (i) *By use of thiophosgene*. The diamine (50 g.) was heated at reflux temperature for 4 hr. with thiophosgene (35 g.; 10% excess) in dry toluene (400 ml.). The crude *solid* obtained on cooling was purified by precipitation with acid from a dilute alkaline solution.

(ii) *By use of carbon disulphide*.[17] A mixture of the diamine (20 g.), carbon disulphide (40 ml.), and dimethylformamide (200 ml.) was heated at 50—60° with stirring for 8 hr. The mixture was then poured into water and the excess of disulphide was boiled off. The *solid* was collected and purified as above to give an 84% yield.

(c) N-*Substituted Benzimidazoles*.—The benzimidazoles were methylated in aqueous alkali with dimethyl sulphate. Other alkyl derivatives (Table 1) were prepared with butyl iodide or prop-2-ynyl bromide in the presence of anhydrous potassium carbonate, in hot cyclohexanone.[25]

4,5,6,7-*Tetrachloro*-1-(*trichloromethylthio*)*benzimidazole*. A solution of 4,5,6,7-tetrachlorobenzimidazole (30 g.) in warm N-sodium hydroxide (700 ml.) was cooled to 20° and stirred with chloroform (300 ml.); trichloromethanesulphenyl chloride (37 g.) was then added dropwise. After 30 min., the organic layer was separated, and the aqueous layer, which contained much undissolved solid, was extracted with more chloroform (2 × 150 ml.). The bulked, dried, organic layers were evaporated under reduced pressure and the residual solid crystallised to give the

[21] H. C. Brimelow, R. L. Jones, and T. P. Metcalfe, *J. Chem. Soc.*, 1951, 1208.
[22] W. Quist, *Acta Acad. Aboensis, Math. Phys.*, 1946, **15**, No. 5, 21.
[23] B.A.S.F., D.R.P. 178,299/1906.
[24] D. F. Kutepov and D. N. Khokhlov, *Zhur. org. Khim.*, 1965, **1**, 191.
[25] G. W. Gray and B. Jones, *J. Chem. Soc.*, 1954, 1467.

product (31 g., 39%) as orange needles, m.p. 182—184° (from ethyl acetate).

Quinoxalines (IV).

(a) *General Procedure.*—The appropriate glyoxal or 1,2-diketone (0·9—1·5 mol.) was added slowly to a hot stirred solution (10%) of the diamine (1 mol.) in ethanol, and the mixture was heated for a further 1—2 hr. The product (Table 2) usually separated rapidly from the hot solution, or crystallised when the mixture was cooled.

A more dilute solution (5%) and longer reaction time (16 hr.) were required for the reaction with benzil. Hydroxyquinoxalines were prepared by use of α-keto-acids or their ethyl esters (Table 2), under the same reaction conditions.

(b) *Chlorination of Quinoxalines.*—*5,6,7,8-Tetrachloro-2-trichloromethylquinoxaline.* An irradiated (150 w, tungsten filament lamp) mixture of the 2-methyl compound (28·2 g.) and sodium acetate (50 g.) in acetic acid (1 l.) was chlorinated for 3·5 hr. at 80—90°. Dilution of the mixture with water gave the *product* (19 g., 49%) as needles, m.p. 186—187° (from acetic acid) (Found: Cl, 64·3. $C_9HCl_7N_2$ requires Cl, 64·4%).

2-Dichloromethyl-3-methyl-5,6,7,8-tetrachloroquinoxaline. Chlorination of 5,6,7,8-tetrachloro-2,3-dimethylquinoxaline (29·6 g.), in acetic acid (500 ml.) containing sodium acetate (50 g.), at 70° for 40 min. yielded the *product* (16·7 g., 45%), m.p. 203—204° (Found: Cl, 58·3. $C_{10}H_4Cl_6N_2$ requires Cl, 58·3%), $\nu_{max.}$ 2995 (CH), 1570 (ring), 1550 (C=N), 1445sh and 1395sh (Me), and 775 (C–Cl) cm.$^{-1}$, τ ($CDCl_3$) 6·85 (3H, s) and 2·72 (s, $CHCl_2$).

2,3-Bisdichloromethyl-5,6,7,8-tetrachloroquinoxaline. Treatment of an irradiated mixture of the 2,3-dimethyl compound (29·6 g.), sodium acetate (50 g.), and acetic acid (1500 ml.) at 80—90° with chlorine gas for 2·5 hr., followed by irradiation for a further 4 hr. at 60—80°, gave the *2,3-bisdichloromethyl derivative* (35·8 g., 82%), m.p. 205—206° (Found: Cl, 65·1. $C_{10}H_2Cl_8N_2$ requires Cl, 65·4%), $\nu_{max.}$ 3020 (CH), 1570 (ring C=C), 1550 (C=N), and 765 (C–Cl) cm.$^{-1}$. N.m.r. showed one singlet only at τ 2·56.

2,5,6,7,8-Pentachloroquinoxaline. 5,6,7,8-Tetrachloroquinoxalin-2(1*H*)-one (41·0 g.), phosphorus pentachloride (31·0 g.), and phosphoryl chloride (150 ml.) were heated with stirring at reflux temperature until the evolution of hydrogen chloride had ceased (1—2 hr.). After 12 hr. the solid was collected, washed thoroughly with carbon tetrachloride, and crystallised to give the *product* (29 g., 66%) as needles, m.p. 168—169° (from ethyl acetate).

Hexachloroquinoxaline. 5,6,7,8-Tetrachloro-1,4-dihydroquinoxaline-2,3-dione (120 g.) and phosphorus pentachloride (165 g., 2 mol.) were heated at reflux temperature for 7—8 hr. in phosphoryl chloride (600 ml.). The reaction mixture was concentrated by distillation and the residue was poured into ice–water. The precipitate was collected and crystallised to give the fully chlorinated *compound* (28·3 g., 21%), m.p. 207—209° (from acetic acid) (Found: Cl, 62·9. $C_8Cl_6N_2$ requires Cl, 63·2%).

(c) *Replacement Reactions.*—*5,6,7,8-Tetrachloro-2-methoxyquinoxaline.* Sodium methoxide [from sodium (1·15 g.) in methanol (100 ml.)] was added to a hot solution of 2,5,6,7,8-pentachloroquinoxaline (15·1 g.) in ethyl acetate (300 ml.). The precipitated solid was collected after a further 30 min., washed with water, dried, and crystallised to give the *product* (7·6 g., 51%), m.p. 180—182° (from ethyl acetate). *5,6,7,8-Tetrachloro-2-ethoxyquinoxaline,* m.p. 171—173°, was similarly obtained by use of sodium ethoxide.

2-Azido-5,6,7,8-tetrachloroquinoxaline. Powdered sodium azid g.) was added to a hot solution of the 2-chloroquin ne (9·3 g.) in dimethylformamide (100 ml.), and the mixture was heated with stirring at 80—90° for 1·5 hr. The solid was collected, washed with water and, after drying, crystallised from benzene to give the *product* (4·0 g., 42%) as light-sensitive fawn needles, decomp. >170°.

Other Systems.

4,5,6,7-Tetrachloro-2,1,3-benzothiazdiazole.—The tetrachloro-*o*-phenylenediamine (24·6 g.) was heated at reflux temperature for 6 hr. with an excess of thionyl chloride (14 g.) in toluene (150 ml.). Removal of the solvents under reduced pressure left a solid, which was crystallised from 2,2,4-trimethylpentane and then acetonitrile to yield the product (21·2 g., 77%), m.p. 159—160° (lit.,[26] 152—154°) (Found: C, 26·6; Cl, 51·9; N, 10·2. Calc. for $C_6Cl_4N_2S$: C, 26·3; Cl, 51·8; N, 10·2%).

6,7,8,9-Tetrachloro-1,3-dihydro-4-methyl-1,5-benzodiazepin-2(2H)-one (X; R^2 = H, R^1 = Cl).—Purified ethyl acetoacetate (14 g.) was added slowly to a hot solution of diamine (24·6 g.) in dry xylene (100 ml.). The mixture was heated under reflux for 1 hr., distilled to half-volume, and cooled. The solid (15·4 g.) was collected, digested with hot ethanol (200 ml.), and crystallised from dioxan to give the *product* (16 g., 50%) (Found: C, 38·6; H, 1·7; Cl, 45·4; N, 8·8. $C_{10}H_6Cl_4N_2O$ requires C, 38·5; H, 1·9; Cl, 45·5; N, 9·0%), $\nu_{max.}$ 3260 (NH), 2950 (CH), 1685 (amide I), 1640 (C=N), and 1440 and 1450sh (CH) cm.$^{-1}$. This compound melted at 260° (preheating to 250°) and then resolidified to a high-melting product, probably 4,5,6,7-tetrachloro-2-methylbenzimidazole.

6,7,8,9-Tetrachloro-1,3-dihydro-1,4-dimethyl-1,5-benzodiazepin-2(2H)-one (X; R^2 = Me, R^1 = Cl).—The above diazepinone and anhydrous potassium carbonate were suspended in dry acetone, and an excess of methyl iodide was added. The mixture was stirred at reflux temperature for 4 hr. and the solid was collected and stirred with water. The insoluble product, m.p. 247—249° (from benzene) (Found: C, 40·6; H, 2·4; Cl, 43·7; N, 8·3. $C_{11}H_8Cl_4N_2O$ requires C, 40·5; H, 2·5; Cl, 43·5; N, 8·6%), was shown to be the *N-methyl compound,* $\nu_{max.}$ 2960 (CH), 1680 (amide I), 1635 (C=N), and 1435 and 1450sh (CH) cm.$^{-1}$, τ ($CDCl_3$) 7·56 (3H, s, 4-Me), 6·76 (3H, s, 1-Me), and 7·05 and 6·51 (2H, CH_2 bridge, AB quartet, *J* 11·5 c./sec.), τ (trifluoroacetic acid) 6·84, 6·49, and 6·14 and 5·66 (*J* 12·8 c./sec.).

4,5,6,7-Tetrachloro-1-hydroxybenzotriazole (III; R = Cl).—Hydrazine hydrate (40%; 20 ml.) and pentachloronitrobenzene (30 g.) in dioxan–ethanol (1 : 1) (120 ml.) were heated for 6 hr. at reflux temperature. Acidification of the deposited hydrazine salt with dilute hydrochloric acid gave the crude product (24·2 g.). Extraction of this material with hot methanol (2 × 250 ml.) and cooling the extracts gave the *product* (9·2 g., 33%), m.p. 208—209°.

4,5,6,7-Tetrachloro-1-hydroxybenzotriazole (5·6 g., 20%) was obtained as a pale brown solid, m.p. 209—210° (decomp.) (from acetic acid) (Found: C, 26·5; H, 0·2; Cl, 52·3; N, 15·1. $C_6HCl_4N_3O$ requires C, 26·4; H, 0·4; Cl, 52·0; N, 15·4%).

An improved preparation (75% yield) of this compound from 3,4,5,6-tetrachloro-1,2-dinitrobenzene will be published later.[12]

[7/1584 *Received, December* 1*st,* 1967]

[26] V. G. Pesin, V. A. Sergeev, and A. M. Khaletskii, *Zhur. obshchei Khim.*, 1964, **34**, 3028.