225. *Seven-membered Heterocyclic Compounds. Part I.* 1 : 5-*Benzodiazepines and Derivatives of* 3 : 6-*Diaza*-4 : 5-*benzotropone.*

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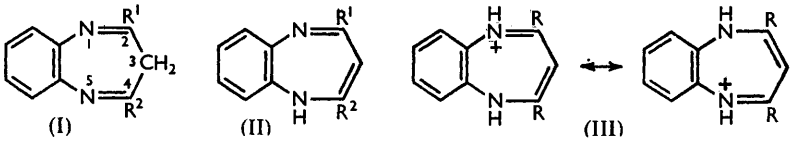
The chemistry, with particular reference to cationoid attack, of 1 : 5-benzodiazepines (I) is discussed. The transformation of 1 : 5-benzodiazepines into derivatives of 3 : 6-diaza-4 : 5-benzotropone, *e.g.*, (VII; R = N·OH), and the reactions of these systems are described.

This investigation was undertaken in order to examine the possibility that there might be a new field of organic chemistry concerned with seven-membered aromatic heterocyclic systems bearing the same relation to pyridine, pyrimidine, etc., as tropone does to benzene. A literature survey suggested that 1 : 5-benzodiazepines (I), readily prepared [1] by condensing *o*-phenylenediamine with β-diketones, were probably the most accessible intermediates for initial experiments.

These substances, though colourless, give rise to intensely purple salts, the colour presumably arising from the resonance canonical forms (III) which are formally analogous to those responsible for the colour of the cyanine dyes.



(I) (II) (III)

Schwarzenbach and Lutz [2] have shown that basification of an aqueous solution of salts containing the cation (III; R = Me) gives, by a very fast reaction, the yellow tautomeric form (II; $R^1 = R^2 = Me$) of the free base which then relatively slowly changes into a colourless form which is either (I; $R^1 = R^2 = Me$) or (IV; R = Me). The free bases, both in the solid state and in organic solvents, exist almost entirely in the di-imino-form (I) because: (i) the infrared spectra of the dimethyl- (I; $R^1 = R^2 = Me$) and the diphenylbenzodiazepine (I; $R^1 = R^2 = Ph$) in Nujol and in $CHCl_3$ show no trace of NH absorption; (ii) the ultraviolet absorption spectrum of the diazepine (I; $R^1 = R^2 = Ph$) is similar to that of benzylideneaniline ($\lambda_{max.}$ 2620, ε 15,500; inflexion 3090 Å, ε 9500) (in EtOH); (iii) the nuclear magnetic resonance spectrum [3] in ethanol of the compound (I; $R^1 = R^2 = Me$) shows only a single absorption band due to the methyl protons, thus indicating a symmetrical molecule: the presence of a CH_2 group in the system is also demonstrated.

It appears that in aqueous solvents also the free bases exist in the di-imino-form, for the ultraviolet absorption spectra of the diphenylbenzodiazepine (I; $R^1 = R^2 = Ph$) in ethanol and in 50% aqueous ethanol are identical (any change in the extinction coefficient of the 258 mμ band is less than 0·2%). For this substance, at least, the evidence is against

[1] Thiele and Steimmig, *Ber.*, 1907, **40**, 955.
[2] Schwarzenbach and Lutz, *Helv. Chim. Acta*, 1940, **23**, 1139.
[3] Barltrop, Richards, and Russell, *J.*, 1959, in the press.

the presence of any detectable amount of the ring-opened form (IV; R = Ph). 1 : 5-Benzodiazepines are unstable systems, their salts in aqueous solution giving reactions characteristic of *o*-phenylenediamine and the β-diketones from which they are derived.

TABLE 1. *Ultraviolet and visible absorption spectra.*

		λ (Å)	ε	λ (Å)	ε
	Quinoxalines				
1	2 : 3-Dimethyl			2370	25900
2	2-Acetyl-3-methyl	2075	28200	2445	32600
3	2-Acetyl-3-methyl oxime	2105	28500	2415	25700
4	2-Acetyl-3-phenyl	2055	31300	2465	34300
5	2-Ethoxycarbonyl-3-phenyl	2135	22800	2435	32700
	1 : 5-*Benzodiazepines*				
6	2 : 4-Dimethyl	2175	25300	2635	6150
7	2 : 4-Dimethyl (hydrogen sulphate) [a]	2240	18500	2595	30200
8	2 : 3 : 4-Trimethyl	2200	25900	2650	6020
9	2 : 3 : 4-Trimethyl (hydrochloride)	2370	15100	2650	20900
10	2 : 4-Diphenyl			2580	45000
11	2 : 4-Diphenyl (hydrochloride)	(2250)	(16500)	(2680)	(21000)
12	2-Methyl-4-phenyl (hydrogen sulphate) [b]	2210	9400	2710	19200
13	2-Methyl-4-*m*-methoxyphenyl (hydrogen sulphate) [b]	2210	14200	2670	17100
14	2-Methyl-4-*p*-methoxyphenyl (hydrogen sulphate) [b]	2300	8900	2670	10800
15	2-Methyl-4-styryl	2100	32600	(2250)	(23000)
16	2-Methyl-4-styryl (hydrochloride)			2750	16800
17	2 : 4-Distyryl			2210	25500
18	2 : 4-Distyryl (hydrochloride)			2820	21100
19	2 : 4-Dimethyl-3-piperonylidene			2580	16300
20	2 : 4-Dimethyl-3-piperonylidene (hydrochloride)				
21	2-Methyl-4-(3 : 4-methylenedioxystyryl)-3-piperonylidene			2540	13700
22	2-Methyl-4-(3 : 4-methylenedioxystyryl)-3-piperonylidene (hydrochloride)				
23	2 : 4-Dimethyl-1-nitroso			2640	14700
24	3-Hydroxyimino-2 : 4-dimethyl	2185	26300		

	λ (Å)	ε	λ (Å)	ε	λ (Å)	ε	λ (Å)	ε	λ (Å)	ε	λ (Å)	ε
1	3160	7200	(3225)	(5600)								
2	3040	6400	(3265)	(5200)								
3	3290	8800	(3465)	(5300)								
4	3315	7400										
5	3315	8500										
6												
7	2685	28400	3255	1150	3345	1100	4940	880	(5735)	(557)	(6315)	(245)
8												
9	2690	20300	(3110)	(1010)			4730	1130				
10	(3350)	(11400)										
11	2910	26600	(3170)	(20000)			5140	1900				
12	3000	13600					5100	1350				
13	2960	12300	3395	5130			5000	1400	5200	1420		
14	2770	10900	3500	10600			5050	1900				
15	3010	31300	(3100)	30200	(3300)	24900						
16	(3460)	(22700)	3740	29100			5480	1440				
17	2990	60000										
18			3970	44000			5800	2800			9030	2210
19	3040	13300	3530	30800								
20	2790	20200	3260	7520	4260	31100						
21	3040	15100	3450	30600								
22	2930	17400	(3030)	(16900)	4390	28700						
23			3090	12000								
24												

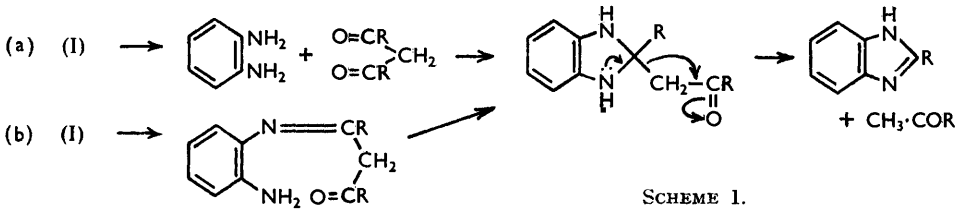
[a] This spectrum was measured on an aqueous solution. [b] These spectra were obtained from methanol solutions.

All other spectra are for solutions in ethanol. Data in parentheses refer to points of inflexion.

For example, salts of 2 : 4-dimethyl-1 : 5-benzodiazepine (I; $R^1 = R^2 = Me$) with diacetyl give 2 : 3-dimethylquinoxaline, and with phenylhydrazine give 3 : 5-dimethyl-1-phenylpyrazole.[1] The diazepinium cations (III; $R^1 = Me$, $R^2 = Me$ or Ph) undergo ring-contraction [1] in warm aqueous solution to the corresponding 2-substituted benziminazoles. Although the simplest picture of these reactions is obtained by postulating complete

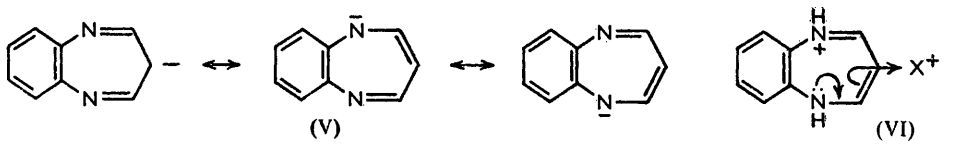
hydrolysis of the diazepine into its components (a, Scheme 1) it seems at least equally probable that the reactions proceed by the fission of one C=N bond only (b, Scheme 1).

On theoretical grounds, one would expect the 1 : 5-benzodiazepines to be susceptible to cationoid attack at position 3, (i) under base-catalysed conditions through the participation of the mesomeric ion (V) and (ii) under acidic conditions through the electromeric displacements (VI). Methyl groups at positions 2 and 4 should also be reactive.



SCHEME 1.

These predictions have experimental support. The diazepine (I; $R^1 = R^2 = Me$), treated in liquid ammonia with sodamide and methyl iodide, gives 2 : 3 : 4-trimethyl-1 : 5-benzodiazepine, m. p. 85°, apparently identical with a compound of m. p. 86° prepared by Vaisman [4] by condensing *o*-phenylenediamine with 3-methylpentane-2 : 4-



(V) (VI)

dione. That methylation occurred, not on the nitrogen atom, but at position 3 follows from the reaction of the compound with phenylhydrazine which gave *o*-phenylenediamine and 3 : 4 : 5-trimethyl-1-phenylpyrazole.

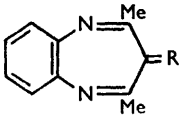
The reaction of the dimethylbenzodiazepine (I; $R^1 = R^2 = Me$) with aromatic aldehydes is more complicated. Benzaldehyde in the presence of aqueous alkali gave a mixture of the methylstyryldiazepine (I; $R^1 = Me$, $R^2 = Ph{\cdot}CH{=}CH$) and the 2 : 4-distyryldiazepine (I; $R^1 = R^2 = Ph{\cdot}CH{=}CH$). In the presence of sodium ethoxide, only the latter compound was obtained. These condensations involving the methyl groups are reversible, for the distyryl partly reverts to the monostyryl derivative on treatment with aqueous alkali. Piperonaldehyde, on the other hand, in the presence of sodium ethoxide or of aqueous alkali, gives the 3-piperonylidene derivative (VII; R = piperonylidene) together with a small amount of the dipiperonylidene derivative (VIII; Ar = $CH_2O_2C_6H_3$).

The positions of the arylidene residues in these compounds were assigned on spectroscopic evidence. Examination of the spectra of all the diazepines in Table 1, which lack a substituent doubly bonded to the 3-position, shows, not only considerable variations in the ultraviolet spectra (which may be partly ascribed to the superimposition on the spectrum of the benzodiazepine nucleus the absorptions due to partial chromophores, *e.g.*, Ph·CH=CH·C=N in Nos. 17 and 18), but also the presence of one common feature—a low-intensity band in the visible region around 5000 Å characteristic of the salts of these compounds and responsible for their intense colours. This feature, which is found in the mono- and di-benzylidene derivatives described above, leads to the suggestion that in these compounds, condensation had occurred on the methyl groups of the dimethylbenzodiazepine. This notion is supported by the infrared spectra of these compounds. The free bases (in Nujol) show strong absorptions at 980 and 967 $cm.^{-1}$ respectively (*trans*-$-CH{=}CH-$) but have no strong band in the region 840—790 $cm.^{-1}$ expected for $>C{=}CH-$. In the electronic spectra of the condensation products with piperonaldehyde, the low-intensity band in the visible region is replaced by a high-intensity band near 4300 Å

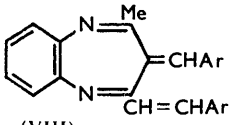
[4] Vaisman, *Trudy Inst. Khim. Kharkov Gosud. Univ.*, 1938, **4**, 157; 1940, **5**, 57; *Chem. Abs.*, 1940, **34**, 5847; 1944, **38**, 750.

(Nos. 20 and 22). This marked change presumably implies a disruption of the resonating system (III) responsible for the colour of 1 : 5-benzodiazepinium salts and, for this reason, a piperonylidene residue is assigned to position 3 in these derivatives.

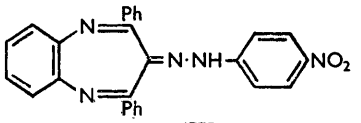
While these compounds are much more stable to hot acid than the parent dimethyldiazepine, the mode of decomposition is similar. The diazepine (VII; R = piperonylidene) gives piperonylideneacetone, 2-methylbenziminazole, and 2-(3 : 4-methylenedioxystyryl)-benziminazole.



(VII)



(VIII)



(IX)

An attempt was also made to prepare the compound (VII; R = Ph·CH=) by condensing *o*-phenylenediamine with 3-benzylidenepentane-2 : 4-dione. With or without acetic acid as catalyst, the product was 2-phenylbenziminazole. With piperidine, 2 : 4-dimethyl-1 : 5-benzodiazepine (I; $R^1 = R^2 = Me$) was obtained, possibly by hydrolysis of the diazepine (VII; R = Ph·CH=). A similar result attended an attempt to prepare 3-acetyl-2 : 4-dimethyl-1 : 5-benzodiazepine by condensing *o*-phenylenediamine with triacetylmethane. Under Thiele and Steimmig's [1] conditions only the dimethyldiazepine was obtained, while heating the components together in benzene afforded a mixture of the dimethyldiazepine, *N*-acetyl-*o*-phenylenediamine, and 2-methylbenziminazole.

Coupling between the *p*-nitrobenzenediazonium cation and the diphenylbenzodiazepine (I; $R^1 = R^2 = Ph$) also occurs in the 3-position, giving what is probably the *p*-nitrophenylhydrazone (IX) of the diphenylbenzotropone. The structure of this compound follows from its infrared spectrum, which shows a NH band. This feature is incompatible with coupling either in the benzene ring or on the NH group of the tautomeric form (II; $R^1 = R^2 = Ph$) of the diazepine. That the substance is the *p*-nitrophenylhydrazone of 2-benzoyl-3-phenylquinoxaline cannot be excluded on present evidence, though the mild conditions of its formation make this unlikely.

1 : 5-Benzodiazepines are clearly not aromatic. The tautomeric form (I) has not the requisite cyclic conjugation and the form (II), though cyclically conjugated, has eight delocalised electrons in its heterocyclic ring (two each from the secondary nitrogen atom and the three double bonds) as against the six required for aromaticity. This lack of aromatic character receives experimental support from the ease with which the nitrogenous ring undergoes fission and ring contraction. By analogy with *cyclo*heptatriene and tropone, aromatic properties might be expected to develop in systems such as (VII; R = O, NR, S, etc.) and the rest of this paper is devoted to a description of experiments on the synthesis of such compounds.

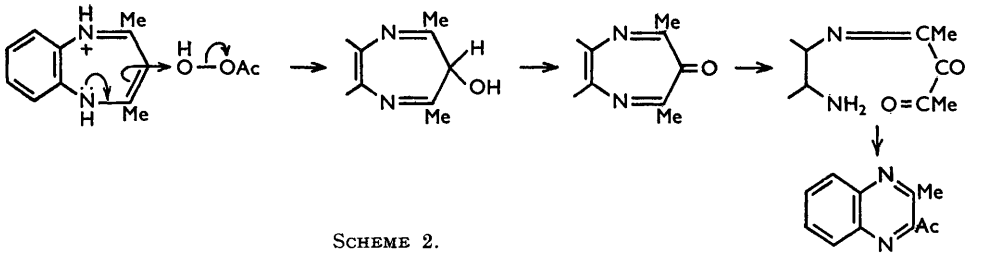
The known susceptibility of 1 : 5-benzodiazepines to cationoid attack suggested that the diazatropone (VII; R = O) might be prepared by oxidising the dimethyldiazepine (I; $R^1 = R^2 = Me$) with per-acids. Both monopersulphuric acid and peracetic acid gave a compound, $C_{11}H_{10}ON_2$, which was found to be identical with a substance which had been prepared [5,6] from *o*-phenylenediamine and pentane-2 : 3 : 4-trione and described as 2-acetyl-3-methylquinoxaline (X). This result alone does not permit a distinction to be made between the 6- and the 7-membered ring formulation. However, we believe the structure (X) to be correct for the following reasons: (i) the carbonyl stretching band in the infrared spectrum lies at 1695 cm.$^{-1}$ in Nujol and 1702 cm.$^{-1}$ in carbon tetrachloride, remote from the 1641 cm.$^{-1}$ band given [7] by 3-benzotropone and near that expected (1700—1680 cm.$^{-1}$) for an aryl methyl ketone; (ii) the ultraviolet spectrum (see Table 1) closely resembles

[5] Piutti, *Gazzetta*, 1936, **66**, 276.
[6] Sachs and Barschall, *Ber.*, 1901, **34**, 3054; Sachs and Röhmer, *Ber.*, 1902, **35**, 3308.
[7] Scott and Tarbell, *J. Amer. Chem. Soc.*, 1950, **72**, 240.

those of authentic quinoxalines; (iii) the nuclear magnetic resonance spectrum [3] of the compound in methanol indicates the presence of two differently situated methyl groups; (iv) a Claisen condensation between ethyl 2-phenylquinoxaline-3-carboxylate and ethyl acetate, followed by hydrolysis of the β-keto-ester, gives a compound identical with that obtained by oxidising 2-methyl-4-phenyl-1 : 5-benzodiazepine with peracetic acid and which from its spectrum and from its method of synthesis must be 2-acetyl-3-phenylquinoxaline.

An interpretation of this oxidative ring-contraction in terms of a hydrolytic equilibrium between the diazepine and acetylacetone, the latter being oxidised to pentane-2 : 3 : 4-trione which then condenses with the diamine to give the acylquinoxaline, seems unlikely since, in a model experiment, no pentanetrione could be isolated on peracetic acid oxidation of acetylacetone, and because, under comparable conditions, peracetic acid reacted with the diazepine many times faster than with acetylacetone. Scheme 2, which postulates the formation and subsequent decomposition of the diazabenzotropone, may be more acceptable, the more so since the diazatropone oxime (VII; R = N·OH) has been shown to undergo an analogous ring-contraction.

A second attempt to prepare derivatives of the diazabenzotropone which involved condensing *o*-phenylenediamine with 3-hydroxyiminopentane-2 : 4-dione was more successful. The components reacted smoothly in benzene to give a compound (A), $C_{11}H_{11}ON_3$, m. p. 215° (decomp.), which must be formulated as the diazabenzotropone oxime (VII; R = N·OH) or as the *cis*- or *trans*-form (XI) of the oxime of 2-acetyl-3-methylquinoxaline, the infrared spectrum indicating the presence of an acidic OH group.



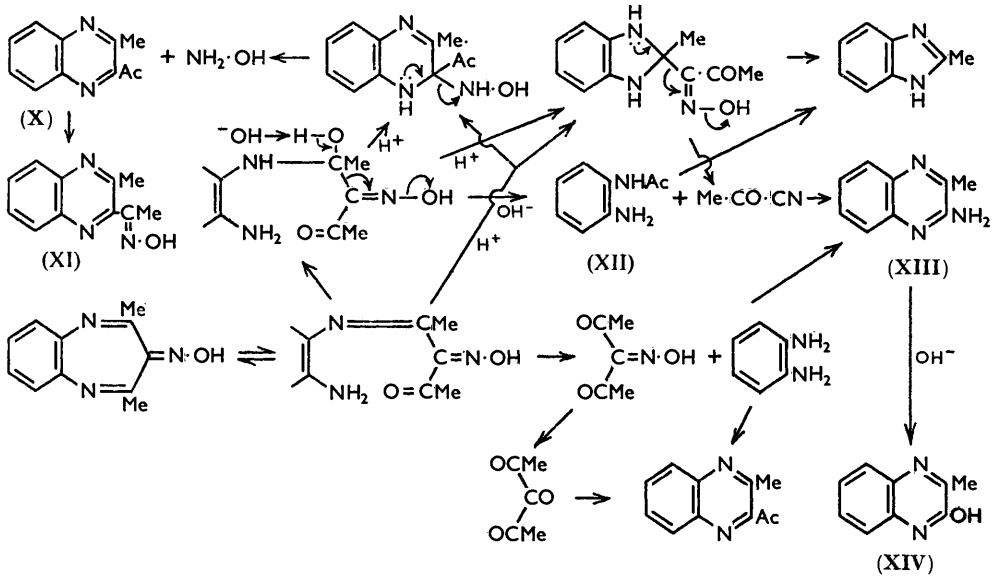
SCHEME 2.

An oxime B, m. p. 196°, of acetylmethylquinoxaline, prepared from the ketone by standard methods, failed to form a chelate compound with cupric acetate and is therefore the form with the N·OH group oriented *anti* with respect to the quinoxaline nucleus. The oxime A although different from this oxime is nevertheless readily transformed into it by treatment with dilute acids. The ultraviolet (see Table 1) and infrared spectra of the oximes A and B differ so profoundly that it is virtually certain that the two compounds cannot be *cis–trans*-isomers and we are led to the conclusion that oxime A is in fact the diazabenzotropone oxime (VII; R = N·OH), a conclusion supported by the pronounced differences in the chemistry of the oximes A and B. Thus, the oxime A on treatment with acetylacetone in the presence of dilute sulphuric acid (but not acetic acid) gives 2 : 4-dimethyl-1 : 5-benzodiazepine sulphate. A similar transformation could not be effected with oxime B.

All attempts to hydrolyse the diazabenzotropone oxime to the diazatropone have been vitiated by ring-contraction. Mineral acids gave oxime B and 2-acetyl-3-methylquinoxaline, while oxalic acid and even acetic acid converted the substance into oxime B and 2-methylbenziminazole.

The diazabenzotropone oxime is also unstable to alkaline reagents. With sodium hydroxide solution it decomposes to, *inter alia*, *o*-phenylenediamine, 2-methylbenziminazole, and 2-hydroxy-3-methylquinoxaline (XIV). With hot sodium carbonate solution it gives the same three products and also *N*-acetyl-*o*-phenylenediamine (XII) and 2-amino-3-methylquinoxaline (XIII). All these transformations may be rationalised in terms of the

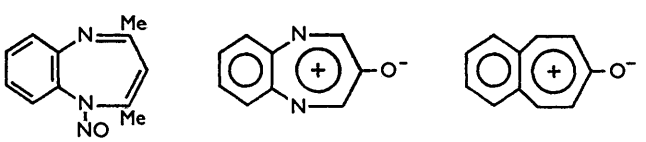
reactions of Scheme 3. The hydroxymethylquinoxaline (XIV) is presumably derived from the aminomethylquinoxaline (XIII) since the latter can be slowly converted into the former by boiling alkali.



SCHEME 3.

An attempt to prepare the diazabenzotropone oxime (VII; R = N·OH) by treating the dimethylbenzodiazepine (I; $R^1 = R^2 = Me$) with sodium nitrite in acetic acid gave, instead, 2-methylbenziminazole and 2-acetyl-3-methylquinoxaline, these compounds presumably being formed through the known rearrangement, by the acetic acid present, of the diazabenzotropone oxime first formed. 2 : 4-Dimethyl-1-nitroso-1 : 5-benzodiazepine (XV) was also formed in this reaction. Its structure is proved by its failure to give intensely coloured salts with acids as would be expected of isomers in which the nitroso-group was located on a methyl group or at position 7, and by its infrared absorption at 1680 $cm.^{-1}$ (in Nujol) (N–N=O; cf. nitrosoguanidine [8] 1653 $cm.^{-1}$). Ozonolysis of the piperonylidene derivative (VII; R = piperonylidene) also failed to yield the required diazabenzotropone—piperonaldehyde was the only identifiable product.

It is quite clear from these results that diazabenzotropone and its derivatives are much more unstable than 3-benzotropone. This is to be expected. Since the ionisation potential of nitrogen is higher than that of carbon, aromatic structures such as (XVI) will be less stable than the corresponding benzotropone structures such as (XVII).



(XV) (XVI) (XVII)

EXPERIMENTAL

2 : 4-*Dimethyl*-1 : 5-*benzodiazepine*.—Acetylacetone (18 c.c.) was added in portions with shaking to a warm solution of *o*-phenylenediamine (19 g.) in ethanol (70 c.c.) and acetic acid (30 c.c.). Concentrated sulphuric acid (25 c.c.) diluted with a little water was added to the violet solution. The precipitated *sulphate* (40 g., 90%) was collected, washed with ethanol and

[8] Lieber, Levering, and Patterson, *Analyt. Chem.*, 1951, **23**, 1594.

with ether, and dried. It formed black-violet needles, m. p. 226° (Found: C, 49·3; H, 5·2; N, 10·8. $C_{11}H_{12}N_2,H_2SO_4$ requires C, 48·9; H, 5·2; N, 10·4%).

2-*Methyl*-4-*phenyl*-1 : 5-*benzodiazepine* (cf. ref. 1).—A solution of *o*-phenylenediamine (2 g.) and benzoylacetone (4 g.) in warm ethanol (8 c.c.) and acetic acid (3 c.c.) was kept at 40° for 30 min., cooled, diluted with ether (20 c.c.), and treated with concentrated sulphuric acid (2·5 c.c.) in water (5 c.c.). The *diazepine hydrogen sulphate monohydrate* (4·9 g., 75%) which separated overnight was collected, washed well with ether, and dried *in vacuo*. It had m. p. 173—175° (Found: C, 54·8; H, 5·1; N, 7·95; S, 9·2. $C_{16}H_{14}N_2,H_2SO_4,H_2O$ requires C, 54·8; H, 5·1; N, 8·0; S, 9·1%).

2-m-*Methoxyphenyl*-4-*methyl*-1 : 5-*benzodiazepine*.—A solution of *o*-phenylenediamine (0·12 g.) and *m*-methoxybenzoylacetone (0·3 g.) in ethanol (2 c.c.) and acetic acid (1 c.c.) was kept at 40° for 90 min. The solution, when cool, was treated with 30% sulphuric acid (4 drops), then cautiously diluted with ether. The *diazepine hydrogen sulphate* (0·19 g.; m. p. 163°), which separated as violet crystals, was collected, washed with ether and dried *in vacuo* (Found: C, 56·0; H, 4·9; N, 7·6; S, 8·6. $C_{17}H_{16}ON_2,H_2SO_4$ requires C, 56·3; H, 5·0; N, 7·7; S, 8·9%).

2-p-*Methoxyphenyl*-4-*methyl*-1 : 5-*benzodiazepine*.—A solution of *p*-methoxybenzoylacetone (1 g.) and *o*-phenylenediamine (0·5 g.) in ethanol (6 c.c.) and acetic acid (1 c.c.) was kept at 40° for 4 hr., then worked up as above. The *diazepine hydrogen sulphate* was obtained as dark violet crystals (1·46 g., 86%), m. p. 191° (Found: C, 55·6; H, 4·8%).

2 : 4-*Diphenyl*-1 : 5-*benzodiazepine* [with G. R.].—*o*-Phenylenediamine (21·6 g.), dibenzoylmethane (44·8 g.), toluene-*p*-sulphonic acid (1·0 g.) and dry xylene (200 c.c.) were boiled together under a Dean–Stark head for 4 hr. and then cooled. 2-Phenylbenziminazole (10 g.), contaminated with a little diphenylbenzodiazepine, separated, having m. p. 287—289° (from methanol) (Found: C, 80·2; H, 5·2; N, 14·7. Calc. for $C_{13}H_{10}N_2$: C, 80·4; H, 5·2; N, 14·4%). Concentration of the filtrate gave the *diphenylbenzodiazepine* (27·0 g., 45%) which formed colourless needles, m. p. 140°, from methanol (Found: C, 85·3; H, 5·6; N, 9·5. $C_{21}H_{16}N_2$ requires C, 85·1; H, 5·4; N, 9·5%), ν (in CS_2) 2900 cm.$^{-1}$ (CH_2), no NH band. The *hydrochloride trihydrate*, m. p. 242—244° (decomp.), was obtained as a violet powder when the hydrochloride, prepared in ether, was dried in air (Found: C, 64·8; H, 5·7; N, 7·1. $C_{21}H_{16}N_2,HCl,3H_2O$ requires C, 65·1; H, 6·0; N, 7·2%). The *hydrochloride monohydrate*, blue-black needles, m. p. 242—244° (decomp.), was obtained by evaporating a solution of the trihydrate in ethanol over sulphuric acid in a desiccator, followed by drying at 78° *in vacuo* (Found: C, 71·2; H, 5·4; N, 8·1; Cl, 10·3. $C_{21}H_{16}N_2,HCl,H_2O$ requires C, 71·8; H, 5·5; N, 8·0; Cl, 10·1%). The *hydrobromide hemihydrate*, a black powder, m. p. 221° after drying *in vacuo* at 110°, was prepared in ethanol and crystallised from ethanol–ether (Found: C, 64·8; H, 4·8; N, 7·5; Br, 20·4. $C_{21}H_{16}N_2,HBr,\frac{1}{2}H_2O$ requires C, 65·1; H, 4·7; N, 7·3; Br, 20·7%). The *picrate* formed coppery-brown needles, m. p. 216—217°, from methanol (Found: C, 60·5; H, 4·1. $C_{21}H_{16}N_2,C_6H_3O_7N_3,CH_3{\cdot}OH$ requires C, 60·3; H, 4·2%).

Condensations effected in ethanolic acetic acid (cf. Thiele and Steimmig [1]) gave much smaller yields.

Reaction of 2 : 4-*Dimethyl*-1 : 5-*benzodiazepine with Diacetyl*.—The diazepine hydrogen sulphate (2 g.) in water (100 c.c.) was shaken with diacetyl (1 c.c.) for 65 hr. until the purple colour had disappeared. 2 : 3-Dimethylquinoxaline (1·05 g.), m. p. 104—106°, was obtained by isolation with ether and distillation of the excess of diacetyl. Recrystallisation from water gave a specimen (0·8 g.), m. p. 106° alone and when mixed with authentic material. The compound and 2 : 3-dimethylquinoxaline had identical infrared spectra.

2-*Acetyl*-3-*methylquinoxaline*.—(*A*) A solution of monopersulphuric acid was prepared by dissolving potassium dipersulphate (13 g.) in concentrated sulphuric acid (16 c.c.) and, after an interval, diluting the mixture with water (40 c.c.). A solution of 2 : 4-dimethyl-1 : 5-benzodiazepine hydrogen sulphate (5 g.) in water (50 c.c.) was added with stirring. When the purple colour had faded (*ca.* 3 hr.), the mixture was basified with sodium hydroxide solution and cooled and the precipitated solid was collected, washed, and dried. 2-Acetyl-3-methylquinoxaline (0·4 g., 12%) crystallised from aqueous ethanol in colourless needles, m. p. and mixed m. p. 87°, giving an intense yellow colour with concentrated sulphuric acid (Found: C, 70·3; H, 5·2; N, 15·2. Calc. for $C_{11}H_{10}ON_2$: C, 71·0; H, 5·4; N, 15·1%). The phenylhydrazone formed needles, m. p. 176°, giving a blue colour in concentrated sulphuric acid. Sachs and Barschall [6] give m. p. 86·5° for the ketone, and Sachs and Röhmer [6] give m. p. 178° for the phenylhydrazone and the same colour reactions. The 2 : 4-*dinitrophenylhydrazone* separated from

acetic acid as orange-red plates m. p. 246—247° (Found: C, 55·4; H, 4·0; N, 23·8. $C_{17}H_{14}O_4N_6$ requires C, 55·7; H, 3·9; N, 23·0%), the oxime as prisms (from aqueous ethanol), m. p. 196° (Found: C, 65·6; H, 5·5; N, 20·4. Calc. for $C_{11}H_{11}ON_3$: C, 65·7; H, 5·5; N, 20·9%) (Sachs and Röhmer [6] give m. p. 194·5°), and the *semicarbazone* as plates, m. p. 247°, from aqueous ethanol (Found: N, 28·6. $C_{12}H_{13}ON_5$ requires N, 28·8%).

(*B*) 12·5% Peracetic acid in acetic acid (450 c.c.) was added slowly to 2 : 4-dimethyl-1 : 5-benzodiazepine hydrogen sulphate (60 g.) dissolved in water (1 l.). After being warmed slightly, the mixture was set aside overnight, then basified and extracted with chloroform. The extracts were dried and evaporated and the residual gum was sublimed at 130—140°/15 mm. The sublimate, crystallised from aqueous ethanol, gave 2-acetyl-3-methylquinoxaline (11 g.), m. p. 87°, alone and when mixed with specimens prepared as above and in accordance with Piutti's directions.[5]

2-*Acetyl*-3-*phenylquinoxaline*.—(*A*) 2-Methyl-4-phenyl-1 : 5-benzodiazepine hydrogen sulphate monohydrate (4 g.) in water (125 c.c.) was oxidised for 3 hr. with peracetic acid solution as described for the previous compound. 2-Acetyl-3-phenylquinoxaline was isolated with chloroform, sublimed at 140—150°/15 mm., and crystallised from ethanol. It formed needles (0·7 g., 35%), m. p. 110° (Found: C, 76·8; H, 4·8; N, 10·9. Calc. for $C_{16}H_{12}ON_2$: C, 77·4; H, 4·9; N, 11·3%). Sachs and Röhmer [6] give m. p. 99·5°; Lutz and Stuart [9] give m. p. 110—111°. The 2 : 4-*dinitrophenylhydrazone* separated from acetic acid in orange-red plates m. p. 223° (Found: C, 61·8; H, 4·0; N, 19·1. $C_{22}H_{16}O_4N_6$ requires C, 61·7; H, 3·8; N, 19·6%).

(*B*) A mixture of ethyl 2-phenylquinoxaline-3-carboxylate (5 g.), ethyl acetate (50 c.c.), and sodium wire (2 g.) was boiled under reflux for 7 hr., poured into ice and dilute hydrochloric acid, and extracted with ether. Distillation of the extracts gave acetoacetic ester (5 c.c.) and a residual gum which was dissolved in ethanol (25 c.c.), boiled under reflux for 18 hr. with concentrated hydrochloric acid (25 c.c.) and water (25 c.c.), diluted with water, and extracted with ether. The extract was washed with 2N-sodium hydroxide solution, dried, and evaporated, and the residue sublimed at 170—190°/15 mm. The sublimate, a mixture of 2-phenylquinoxaline and 2-acetyl-3-phenylquinoxaline (2·54 g.), was dissolved in light petroleum and chromatographed over alumina (170 g.). 2-Phenylquinoxaline (1·78 g.), which came off the column first, when crystallised from light petroleum (b. p. 40—60°), formed crystals (1·45 g.), m. p. 77—78° (Found: C, 81·8; H, 4·8; N, 13·1. Calc. for $C_{14}H_{10}N_2$: C, 81·5; H, 4·9; N, 13·6%). Fischer and Römer [10] give m. p. 78°. Further development of the column with light petroleum gave 2-acetyl-3-phenylquinoxaline (0·73 g.), which separated from light petroleum (b. p. 40—60°) in crystals (0·62 g.), m. p. and mixed m. p. 111—112° (Found: C, 77·1; H, 4·9; N, 11·7. Calc. for $C_{16}H_{12}ON_2$: C, 77·4; H, 4·9; N, 11·3%). The sodium hydroxide washings when acidified and extracted with ether gave 2-hydroxy-3-phenylquinoxaline, which when recrystallised from aqueous ethanol gave crystals (0·62 g.), m. p. 252° (Buraczewski and Marchlewski [11] give m. p. 247°) (Found: C, 75·7; H, 4·9; N, 12·3. Calc. for $C_{14}H_{10}ON_2$: C, 75·7; H, 4·5; N, 12·6%).

2 : 3 : 4-*Trimethyl*-1 : 5-*benzodiazepine*.—2 : 4-Dimethyl-1 : 5-benzodiazepine (3 g.) in dry tetrahydrofuran (20 c.c.) was added to a stirred solution of sodamide [from sodium (0·4 g.)] in liquid ammonia (150 c.c.), and after 15 min. methyl iodide (5·0 g.) was added dropwise. The stirring was continued for a further 15 min. and the ammonia was allowed to evaporate. The residue was treated with water and the product, an oil (3·01 g.) which crystallised, was isolated with ether. Sublimation at 85—90°/0·05 mm. gave the trimethylbenzodiazepine (2·74 g.), m. p. 85°, from light petroleum (Found: C, 76·9; H, 7·8; N, 15·5. Calc. for $C_{12}H_{14}N_2$: C, 77·4; H, 7·6; N, 15·0%).

Reaction of 2 : 3 : 4-*Trimethyl*-1 : 5-*benzodiazepine with Phenylhydrazine*.—The diazepine (470 mg.) in ethanol (10 c.c.) was shaken with a solution of phenylhydrazine (0·25 c.c.) in concentrated hydrochloric acid (0·2 c.c.) and water (5 c.c.) until the deep red colour was discharged (2 hr.), then poured into water. Isolation with ether gave an oil, which on distillation at 195—200° (bath temp.)/24 mm. gave 3 : 4 : 5-trimethyl-1-phenylpyrazole (250 mg.) [picrate (from ethanol), m. p. 115° (lit.,[12] m. p. 116°)]. The aqueous solution, after basification and extraction

[9] Lutz and Stuart, *J. Amer. Chem. Soc.*, 1937, **59**, 2316.
[10] Fischer and Römer, *Ber.*, 1908, **41**, 2350.
[11] Buraczewski and Marchlewski, *Ber.*, 1901, **34**, 4009.
[12] Knorr and Jochheim, *Ber.*, 1903, **36**, 1277.

with ether, gave an oil, which on sublimation at 120—130°/20 mm. afforded *o*-phenylenediamine (110 mg.), m. p. and mixed m. p. 101—102° (from benzene–light petroleum).

Reaction of 2 : 4-*Dimethyl*-1 : 5-*benzodiazepine with Piperonaldehyde.*—(*A*) The diazepine (5·0 g.), piperonaldehyde (4·35 g.), and dry ethanol (150 c.c.) were boiled together for 40 min. in the presence of sodium ethoxide (from sodium, 0·66 g.). After ethanol (50 c.c.) had been distilled, the boiling mixture was filtered. 2-*Methyl*-4-(3 : 4-*methylenedioxystyryl*)-3-*piperonylidene*-1 : 5-*benzodiazepine* (670 mg.) was collected and crystallised from benzene, from which it separated in yellow needles, m. p. 257—258° (Found: C, 74·1; H, 4·7; N, 6·5. $C_{27}H_{20}O_4N_2$ requires C, 74·3; H, 4·6; N, 6·4%), ν (in Nujol) 1627 cm.$^{-1}$. The substance gives a dark brown colour with acids. The filtrate, when kept overnight, deposited yellow 2 : 4-*dimethyl*-3-*piperonylidene*-1 : 5-*benzodiazepine* (2·74 g.), m. p. 192—193° (from benzene–light petroleum) (Found: C, 75·0; H, 5·2; N, 8·9. $C_{19}H_{16}O_2N_2$ requires C, 75·0; H, 5·3; N, 9·2%), ν (in Nujol) 1628 cm.$^{-1}$. The substance gives a dark brown colour with acid.

(*B*) The diazepine (2·0 g.) and aldehyde (1·74 g.) in ethanol (100 c.c.) were set aside for 20 days in the presence of saturated aqueous potassium hydroxide solution (0·3 c.c.), then diluted with water. The product, when isolated with ether and chromatographed in 1 : 1 benzene–light petroleum on alumina, gave piperonaldehyde (460 mg.), 2 : 4-dimethyl-3-piperonylidene-1 : 5-benzodiazepine (1·85 g.), and the dipiperonylidene derivative (40 mg.).

Reaction of 2 : 4-*Dimethyl*-1 : 5-*benzodiazepine with Benzaldehyde.*—(*A*) The diazepine (5 g.) and benzaldehyde (3·1 c.c.) in ethanol (100 c.c.) were boiled under reflux for 1 hr. in the presence of sodium ethoxide (from sodium 0·66 g.). Benzaldehyde (3·1 c.c.) was added and boiling was continued for a further 3 hr. The mixture was concentrated to small bulk, then poured into water, and the oily product (10·5 g.) was isolated with ether and chromatographed on alumina (400 g.) in 1 : 1 benzene–light petroleum. The oil (4·94 g.) so obtained when crystallised from benzene–light petroleum gave 2 : 4-*distyryl*-1 : 5-*benzodiazepine* (2·29 g.), yellow needles, m. p. 164—165° (Found: C, 86·2; H, 5·9; N, 7·8. $C_{25}H_{20}N_2$ requires C, 86·2; H, 5·8; N, 8·0%), ν (in Nujol) 1628 cm.$^{-1}$ (C=C). The substance gives a green solution in acids.

(*B*) The diazepine (6 g.) and benzaldehyde (3·6 c.c.) in ethanol (200 c.c.) were kept for 18 days in the presence of saturated aqueous potassium hydroxide (1 c.c.). The oily product, isolated as in previous experiments, was chromatographed on alumina (600 g.) in 1 : 1 benzene–light petroleum, thus yielding 2 : 4-distyryl-1 : 5-benzodiazepine (2·55 g.), m. p. 164—165° after crystallisation, followed by a sticky solid (3·01 g.) which when crystallised from benzene–light petroleum gave 2-*methyl*-4-*styryl*-1 : 5-*benzodiazepine* (2·14 g.), m. p. 128—129° (Found: C, 82·7; H, 5·9; N, 11·0. $C_{18}H_{16}N_2$ requires C, 83·0; H, 6·2; N, 10·8%), ν (in Nujol) 1630 cm.$^{-1}$. The substance gives a purple colour with acids.

Hydrolysis of 2 : 4-*Distyryl*-1 : 5-*benzodiazepine.*—The diazepine (500 mg.) in ethanol (30 c.c.) was set aside for 8 days with saturated aqueous potassium hydroxide (0·3 c.c.). The product, in 1 : 1 benzene–light petroleum, was chromatographed on alumina, giving successively starting material (130 mg.) and 2-methyl-4-styryl-1 : 5-benzodiazepine (100 mg.), m. p. 128—129° (from benzene–light petroleum).

Reaction of 2 : 4-*Dimethyl*-3-*piperonylidene*-1 : 5-*benzodiazepine with Acid.*—The diazepine (500 mg.) in ethanol (20 c.c.) was heated under reflux with concentrated hydrochloric acid (0·15 c.c.) until the dark brown colour faded (18 hr.). The solution was basified and the solid obtained by isolation with ether was triturated with benzene (15 c.c.). The insoluble material gave 2-(3 : 4-*methylenedioxystyryl*)*benziminazole* (55 mg.), m. p. 220—221° (from aqueous methanol) (Found: C, 73·0; H, 4·8; N, 10·5. $C_{16}H_{12}O_2N_2$ requires C, 72·7; H, 4·6; N, 10·6%). The infrared spectrum (in Nujol) showed the typical broad associated NH band of benziminazoles and a peak at 1255 s cm.$^{-1}$ (aryl ether). The benzene-soluble material was separated by crystallisation from benzene–light petroleum into 2-methylbenziminazole (90 mg.), m. p. and mixed m. p. 174—175°, and piperonylideneacetone (60 mg.), m. p. and mixed m. p. 110°.

Condensation of Benzylideneacetylacetone with o-*Phenylenediamine.*—Benzylideneacetylacetone (5 g.) and *o*-phenylenediamine (2·87 g.) in benzene (60 c.c.) were heated under reflux for 4 hr. with piperidine (0·3 c.c.). Distillation of solvent gave an oil which, chromatographed on alumina in 1 : 1 benzene–light petroleum, gave successively a semi-solid oil (3·31 g.) which yielded 2-phenylbenziminazole (1·15 g.), m. p. 287—289° (from aqueous methanol), and an oil (1·32 g.) which afforded 2 : 4-dimethyl-1 : 5-benzodiazepine (620 mg.), m. p. and mixed m. p. 131—132°, on crystallisation from benzene–light petroleum.

Similar condensations effected either in boiling toluene without catalyst, or in ethanol–acetic acid at 50°, gave only 2-phenylbenziminazole and *o*-phenylenediamine.

Condensation of o-*Phenylenediamine with Triacetylmethane.*—(*A*) Triacetylmethane (2·5 g.) in ethanol (5 c.c.) and a solution of *o*-phenylenediamine (1·9 g.) in ethanol (7 c.c.) and acetic acid (3 c.c.) were mixed and the resulting violet solution was poured into sulphuric acid (2·5 c.c.) in water (30 c.c.). After 1 hr., 2 : 4-dimethyl-1 : 5-benzodiazepine sulphate (1·44 g.) was collected. It was characterised as the free base, m. p. and mixed m. p. 131—132°.

(*B*) Triacetylmethane (1·5 g.) and *o*-phenylenediamine (1·16 g.) in benzene (75 c.c.) were boiled under reflux for 1½ hr., concentrated to small bulk, then poured into water, and the product, an oil (1·99 g.), was isolated with ether. The oil, washed with 1 : 1 benzene–light petroleum (100 c.c.) left as an insoluble residue *N*-acetyl-*o*-phenylenediamine (250 mg.), m. p. and mixed m. p. 132—133°. The washings, chromatographed on alumina and eluted with benzene, gave 2 : 4-dimethyl-1 : 5-benzodiazepine (350 mg.). Elution with ether gave an oil, which when rechromatographed on alumina and eluted with benzene gave 2-methylbenziminazole (130 mg.), m. p. and mixed m. p. 174—175°. Elution with ether then gave more *N*-acetyl-*o*-phenylenediamine (255 mg.).

3-*Oxo*-2 : 4-*diphenyl*-1 : 5-*benzodiazepine* p-*Nitrophenylhydrazone* [with G. R.].—*p*-Nitroaniline (0·23 g.) in concentrated hydrochloric acid (1 c.c.) and water (5 c.c.) was diazotised at 0° and poured into an ice-cold solution of diphenylbenzodiazepine (0·5 g.) in ethanol (100 c.c.), then treated with a solution of sodium acetate (1·0 g.). Dilution with water gave a brown flocculent precipitate (0·59 g.), which was collected, washed with water, and chromatographed on alumina. Elution with 1 : 10 benzene–light petroleum gave unchanged diphenylbenzodiazepine (0·27 g.). 1 : 1 Benzene–light petroleum eluted the p-*nitrophenylhydrazone* (0·26 g.), a yellow powder (from aqueous ethanol), m. p. 252—253° (Found: C, 73·0; H, 4·8; N, 15·7. $C_{27}H_{19}O_2N_5$ requires C, 72·8; H, 4·3; N, 15·7%), ν (in Nujol) 3300 cm.$^{-1}$ (NH), which gives a yellow colour with hydrochloric acid.

3-*Hydroxyimino*-2 : 4-*dimethyl*-1 : 5-*benzodiazepine.*—*o*-Phenylenediamine (40 g.) and 3-hydroxyiminopentane-2 : 4-dione (40 g.) were refluxed in benzene (400 c.c.) for 1 hr. The *diazatropone oxime* (60 g.), which separated on cooling, was collected and crystallised from methanol. It formed colourless needles, m. p. 215° (decomp.) (Found: C, 65·5; H, 5·5; N, 20·2. $C_{11}H_{11}ON_3$ requires C, 65·7; H, 5·5; N, 20·9%).

Reaction between Acetylacetone and 3-*Hydroxyimino*-2 : 4-*dimethyl*-1 : 5-*benzodiazepine.*—A solution of the oxime (0·5 g.) and acetylacetone (2 c.c.) in ethanol (20 c.c.) at 50° was treated with 2N-sulphuric acid (10 c.c.). An intense purple colour developed immediately. Next morning, the solution was diluted with water (50 c.c.) and washed with ether. The aqueous solution contained 2 : 4-dimethyl-1 : 5-benzodiazepine, identified spectroscopically ($\lambda_{max.}$ 4940 with inflexions at 6315 and 5735 Å) and by boiling the solution until colourless, whereafter basification of the solution followed by isolation with ether gave 2-methylbenziminazole (200 mg.), m. p. 174°, after crystallisation from benzene–ligroin.

Acid Hydrolysis of 3-*Hydroxyimino*-2 : 4-*dimethyl*-1 : 5-*benzodiazepine.*—(*A*) The oxime (2 g.) was heated for 30 min. on the steam-bath with 10% sulphuric acid (120 c.c.) and ferric chloride (1·6 g.), then cooled and extracted with ether. The extracts yielded a gum which was sublimed. 2-Acetyl-3-methylquinoxaline (0·4 g.) was isolated at 130—140°/15 mm.; it had m. p. and mixed m. p. 87° (from aqueous ethanol). Sublimation at 170—180°/15 mm. gave 2-acetyl-3-methylquinoxaline oxime (0·3 g.), m. p. and mixed m. p. 196° (from ethanol).

(*B*) The oxime (500 mg.) in ethanol (15 c.c.) and acetic acid (15 c.c.) was kept at room temperature for 30 hr., then poured into water and extracted with ether. The extract was washed with sodium carbonate solution and evaporated and the product was sublimed at 170—180°/17 mm. 2-Acetyl-3-methylquinoxaline oxime (130 mg.), was obtained having m. p. and mixed m. p. 196° (from aqueous methanol). Basification of the aqueous solution and isolation with ether gave 2-methylbenziminazole (80 mg.), m. p. and mixed m. p. 174—175° (from benzene).

Alkaline Hydrolysis of 3-*Hydroxyimino*-2 : 4-*dimethyl*-1 : 5-*benzodiazepine.*—(*A*) Sodium hydroxide (2·5 g.) and the oxime (5 g.) in water (100 c.c.) were heated on the steam-bath for 17 hr. Ammonia was evolved during the reaction. The solution was extracted with ether, yielding a solid (1·75 g.) which was dissolved in 1 : 1 benzene–light petroleum and chromatographed on alumina. This gave, successively, an orange primary amine (40 mg.), m. p. 135—136° (from benzene–light petroleum), *o*-phenylenediamine (950 mg.), and 2-methylbenziminazole

(350 mg.). The aqueous reaction mixture, when acidified and extracted with ether, gave a brown solid, which on sublimation at 180—190°/15 mm. and crystallisation from aqueous methanol gave 2-hydroxy-3-methylquinoxaline (70 mg.), m. p. 240—242° (Hinsberg [13] gives m. p. 245°) (Found: C, 67·1; H, 5·1; N, 17·0. Calc. for $C_9H_8ON_2$: C, 67·5; H, 5·0; N, 17·5%), ν (in Nujol) 1668 cm.$^{-1}$. 2-Hydroxy-3-phenylquinoxaline has ν 1665 cm.$^{-1}$.

(*B*) The oxime (5 g.) in ethanol (120 c.c.), and sodium carbonate (3·75 g.) dissolved in water (150 c.c.), were heated together on a steam-bath for 2 hr., then cooled. The solid product (2·35 g.) was isolated with ether and extracted with boiling benzene (100 c.c.), giving 2-methylbenziminazole (740 mg.) as an insoluble residue. The benzene extract was adsorbed on an alumina column. Elution with 1 : 1 benzene–light petroleum gave a mixed fraction from which *o*-phenylenediamine (40 mg.), m. p. and mixed m. p. 101—102°, sublimed at 120—130°/20 mm., leaving as an involatile residue 2-amino-3-methylquinoxaline (320 mg.), m. p. and mixed m. p. 166—167° (from benzene–light petroleum) (Found: C, 67·5; H, 6·0; N, 25·9. Calc. for $C_9H_9N_3$: C, 67·9; H, 5·7; N, 26·4%), ν (in Nujol) 3470, 3300 cm.$^{-1}$ (NH_2). Continued elution gave more aminomethylquinoxaline (350 mg.). Elution with 1 : 10 ether–benzene gave 2-methylbenziminazole (240 mg.), m. p. and mixed m. p. 174—175°, 2-hydroxy-3-methylquinoxaline (90 mg.), m. p. 240—242°, and *N*-acetyl-*o*-phenylenediamine (90 mg.), m. p. and mixed m. p. 132—133° (from benzene–light petroleum).

Hydrolysis of 2-*Amino*-3-*methylquinoxaline*.—The quinoxaline (170 mg.) in ethanol (10 c.c.) was heated on the steam-bath with 2N-sodium hydroxide (5 c.c.) for 3 hr. Starting material (140 mg.) was isolated with ether. The aqueous solution, when acidified and extracted with ether, yielded 2-hydroxy-3-methylquinoxaline (15 mg.), m. p. and mixed m. p. 240—242°, infrared spectrum identical with that of an authentic specimen. Similar results were obtained from a hydrolysis performed with aqueous sodium carbonate.

Nitrosation of 2 : 4-*Dimethyl*-1 : 5-*benzodiazepine*.—Sodium nitrite (1·86 g.) in water (15 c.c.) was added with stirring to the diazepine (2 g.) in ethanol (40 c.c.) and acetic acid (25 c.c.) at 5°. After 10 days at room temperature, the mixture was basified with sodium carbonate solution, and the product isolated with ether, dissolved in 1 : 1 benzene–light petroleum, and chromatographed on alumina. Elution with this solvent gave 2-acetyl-3-methylquinoxaline (300 mg.), m. p. and mixed m. p. 86° (from light petroleum), followed by 2 : 4-*dimethyl*-1-*nitroso*-1 : 5-*benzodiazepine* (180 mg.), pale yellow needles, m. p. 80° (from light petroleum) (Found: C, 65·6; H, 5·7; N, 20·9. $C_{11}H_{11}ON_3$ requires C, 65·7; H, 5·5; N, 20·9%). The latter substance gives a yellow solution with acids. Elution with ether yielded 2-methylbenziminazole (270 mg.), m. p. and mixed m. p. 174—175°.

Ozonolysis of 2 : 4-*Dimethyl*-3-*piperonylidene*-1 : 5-*benzodiazepine*.—The diazepine (500 mg.) in ethyl acetate (20 c.c.) and acetic acid (30 c.c.) was ozonised at 0° with 2% ozonised oxygen containing 1·6 mol. of ozone. The solution was flushed with nitrogen, water (30 c.c.) was added, and after 18 hr. the mixture was diluted with water and extracted with ether. The ether extract, on chromatography, gave only piperonaldehyde (50 mg.), identified as the 2 : 4-dinitrophenylhydrazone, m. p. 275—277° (decomp.) (from acetic acid). The aqueous reaction mixture when basified and extracted with ether gave only unchanged diazepine (80 mg.).

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[13] Hinsberg, *Annalen*, 1896, **292**, 249.