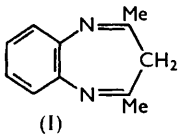
278. *The Reduction of 2-Acetyl-3-methylquinoxaline and 2 : 4-Dimethyl-1 : 5-benzodiazepine.*

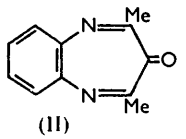
By J. A. Barltrop, C. G. Richards, and (in part) D. M. Russell.

Catalytic reduction of 2-acylquinoxalines gives deeply coloured products, which are shown to be 1 : 4-dihydro-derivatives (X) ⟷ (XIII). The oxidation, dismutation, and further reduction of the compound (XIII; R = Me) are described. The application of nuclear magnetic resonance spectra to the determination of the structures of this compound and of the *cis*- (XIX) and the *trans*-form (XX) of 1 : 2 : 4 : 5-tetrahydro-2 : 4-dimethyl-1 : 5-benzodiazepine is illustrated.

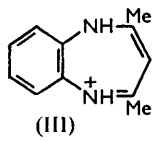
Barltrop, Richards, Russell, and Ryback have shown [1] that oxidation of 2 : 4-dimethyl-1 : 5-benzodiazepine (I) with per-acids leads to 2-acetyl-3-methylquinoxaline (IV; R = Me). During the early stages of this investigation, when it was thought that the product was the required benzodiazatropone (II), the ketone was hydrogenated in order to obtain the 3-hydroxy-1 : 5-benzodiazepine (V; R = Me).



(I)



(II)



(III)

Uptake of hydrogen was rapid over palladised charcoal and slower over Raney nickel, giving a deep crimson solution, which, under acidic conditions, assumed an intense violet colour. Reduction with tin or zinc and acid produced the same violet solution. The solutions were unstable in air, rapidly reoxidising to 2-acetyl-3-methylquinoxaline (IV; R = Me).

Stafford and Barker [2] also studied the reduction of the ketone (IV; R = Me) and reported that hydrogenation proceeds with the uptake of one *g.-atom* of hydrogen per mole giving an intensely red solution. From this and related observations they ascribe a free-radical structure to the red reduction product.

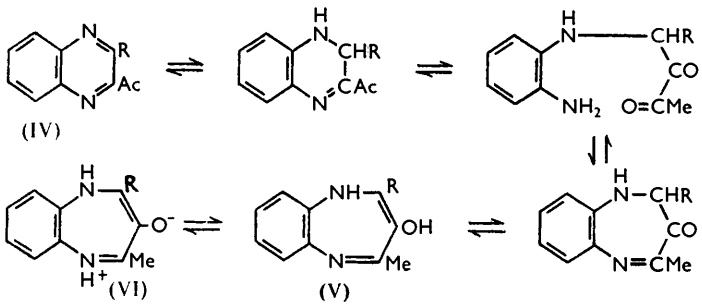
Our results differ from those of Stafford *et al.* First, with palladised charcoal and with Raney nickel, hydrogenation proceeded with no detectable break until one *mol.* of hydrogen had been absorbed. Secondly, the red solution, examined as a 0·53M-solution, was found to be diamagnetic, thus excluding the possibility that it contained any significant concentration of radical. Even when hydrogenation was stopped after the uptake of one *atom* of hydrogen, the solution was again diamagnetic. Thirdly, the dye has been isolated as red-brown needles with the analysis $C_{11}H_{12}ON_2$ expected for a dihydro-derivative. The possibility that these red needles were a dismutation product of the red component of the hydrogenated solution was eliminated by the observation that the visible spectrum of the latter was identical with that of a solution prepared from this red solid. Similar results were obtained with 2-acetyl-3-phenylquinoxaline (IV; R = Ph), from the reduction of which a purple-red dye was isolated. The infrared spectra of the solid reduction product of the methyl derivative (IV; R = Me) in Nujol showed NH or OH peaks at 3320 and 3220 cm.$^{-1}$ (as fine structure superimposed on a broad band of the type commonly ascribed to associated NH or OH groups) and C–O stretching at 958 cm.$^{-1}$, but no carbonyl group. The solid dyes were stable in air for several days.

It is clear from these results that the coloured reduction products are dihydro-derivatives of the 2-acetylquinoxalines. The dihydro-derivative (IX), which was prepared by borohydride reduction of the ketone (IV; R = Me) and was also obtained by Stafford,

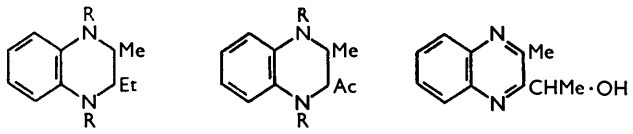
[1] Barltrop, Richards, Russell, and Ryback, *J.*, 1132.
[2] Stafford and Barker, *Chem. and Ind.* 1956, 1426.

Reid, and Barker [3] by a Pondorff reduction, is a colourless solid and can be transformed into a red dye neither by acid-treatment nor by further reduction. It is likely, therefore, that reduction must occur in the heterocyclic ring if colour is to be developed.

Since the instability of the reduction products to hot dilute acid and their visible spectra were reminiscent of benzodiazepinium salts,[1] we originally proposed [4] that the reduction products were betaines (VI) derived from 3-hydroxy-1 : 5-benzodiazepines (V), possibly formed by the sequence of reversible reactions shown in the annexed formulæ.



This hypothesis now appears to be incorrect for the following reasons.* First, 2 : 4-dimethyl-1 : 5-benzodiazepine (I) is a relatively weak base,[5] so that the proton-transfer involved in the conversion of the colourless hydroxybenzodiazepine (V) into the coloured betaine is improbable. Secondly, benzodiazepinium cations appear [1,6] to be in hydrolytic equilibrium with *o*-phenylenediamine and the corresponding β-diketones, reacting with phenylhydrazine to give the appropriate phenylpyrazoles. The reduction product derived from the ketone (IV; R = Me), however, undergoes a redox reaction with phenylhydrazine giving aniline and the phenylhydrazone of the initial ketone. Thirdly, although 2 : 4-



dialkyl-1 : 5-benzodiazepines undergo ring-contraction to 2-alkylbenziminazoles when warmed in acid solution, the reduction product derived from the ketone (IV; R = Me), under similar conditions, gives no 2-methylbenziminazole but only small amounts of the *cis*- and the *trans*-form of 2-ethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline, isolated as their dibenzoyl derivatives (VII; R = Bz). Further, the postulated ring-expansion to the seven-membered betaine requires the participation of water. This substance is not involved since the ketone (IV; R = Me) in dry light petroleum over palladised charcoal rapidly absorbed one mol. of hydrogen, giving a colourless solution with the red reduction product adsorbed on the catalyst from which it could be eluted with dry ethanol or dry dioxan.

That the red dye is a dihydroquinoxaline became probable when it was found that in boiling ethanol, under nitrogen, in the presence but not the absence of palladised charcoal, it underwent dismutation to a mixture of 2-acetyl-3-methylquinoxaline, 2-acetyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline (VIII; R = H), and 2-1′-hydroxyethyl-3-methylquinoxaline (IX). Chromatography showed the absence of these products from the

* We are indebted to a Referee for helpful comment on some of these points.

[3] Stafford, Reid, and Barker, *Chem. and Ind.*, 1956, 765.
[4] Barltrop and Richards, *ibid.*, 1957, 1011.
[5] Schwarzenbach and Lutz, *Helv. Chim. Acta*, 1940, **23**, 1159.
[6] Thiele and Steimmig, *Ber.*, 1907, **40**, 955.

ethanol solution before the heating. Proof of the six-membered ring structure for the coloured reduction product of the ketone (IV; R = Me) was obtained from a study of the nuclear magnetic resonance spectrum of the dyestuff (all such spectra were measured at 29·92 Mc.p.s, the accuracy of the measurements being 5% or better). Unlike a dihydroquinoxaline, the diazepinium betaine formulation (VI) has a symmetrical distribution of methyl groups and would therefore be expected to have one methyl proton resonance absorption only. 2 : 4-Dimethyl-1 : 5-benzodiazepine (I) and the ketone (IV; R = Me) were taken as models for the alternative structures. The spectrum of the former (I) (Fig. 1) showed a single intense band due to the six identical protons of its methyl groups 1·1

FIG. 1.

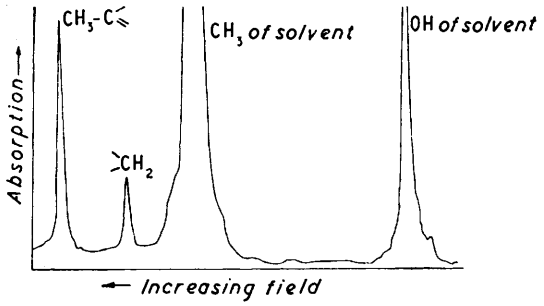
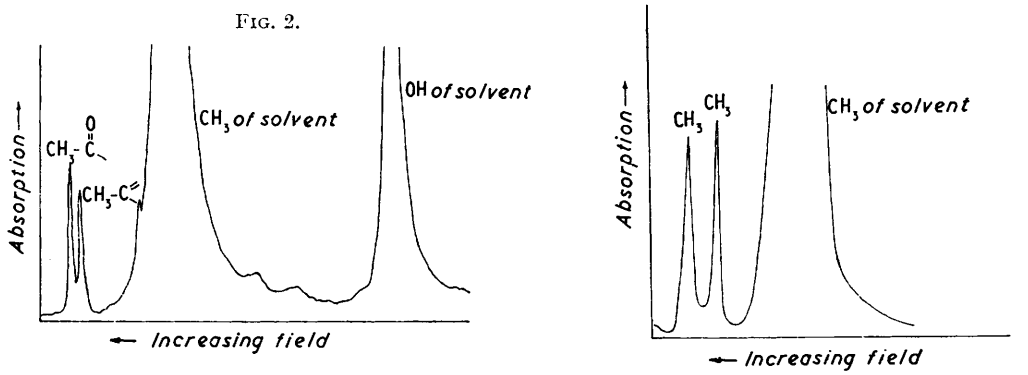


FIG. 3.

FIG. 2.

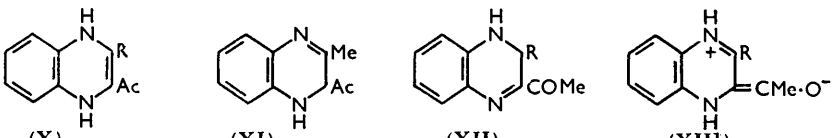


Nuclear magnetic resonance spectra of (FIG. 1) *2 : 4-dimethyl-1 : 5-benzodiazepine,* (FIG. 2) *2-acetyl-3-methylquinoxaline, both in methanol, and* (FIG. 3) *2-acetyl-1 : 4-dihydro-3-methylquinoxaline, in dimethylformamide.*

parts per million (p.p.m.) from the methyl absorption of the solvent methanol. The spectrum (Fig. 2) of the ketone (IV; R = Me) had two bands 0·07 p.p.m. apart, the one at lower field strength being 0·6 p.p.m. from the methyl absorption of the solvent, the methyl groups having different environments in this molecule. The reduction product in dimethylformamide had two methyl absorption bands 0·3 p.p.m. apart, the one at lower field strength being 0·7 p.p.m. from the solvent methyl band (Fig. 3) which is itself displaced 0·6 p.p.m. towards higher fields from the methyl band of methanol. The reduction product is therefore a dihydroquinoxaline. Of the three structures possible for such a system the isomer (XII; R = Me) can be eliminated on the grounds that it should give rise to three methyl bands: a singlet due to the $CH_3{\cdot}CO$ grouping and a doublet due to the splitting of the methyl band of the group $CH_3{\cdot}CH<$ by the adjacent single proton. The relative intensities of these bands would be 2 : 1 : 1. Structures (X; R = Me) and (XI) are both consistent with the number and relative intensities of the methyl absorption

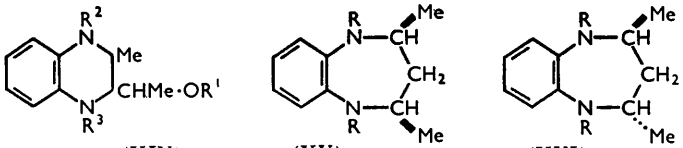
bands found in the nuclear magnetic resonance spectrum of the reduction product, but the latter structure affords no adequate explanation of the colour. We must therefore conclude that, in dimethylformamide, the reduction product exists mainly, or even exclusively, in the form (X; R = Me), the colour presumably arising from resonance with the polar canonical form (XIII). However, on present evidence, one cannot exclude the possibility that the tautomeric forms (XI) and (XII; R = Me) may contribute significantly in other solvents or under other conditions. The coloured reduction product derived from 2-acetyl-3-phenylquinoxaline is, by analogy, assigned the structure (X ⟷ XIII; R = Ph).

The relative positions of the absorption bands due to the methyl groups in the above nuclear magnetic resonance spectra are explicable on the basis that an increase of electron density in the vicinity of such a group causes shielding which is manifested by a displacement of the band in the direction of increasing field strength. Thus, the greater separation of the two methyl bands in the reduction product (X ⟷ XIII; R = Me) by comparison



with the initial ketone (IV; R = Me) is attributable to the greater negative charge on the carbonyl-oxygen atom in the former, which leads to a shift to higher fields. Also the electrophilic character of aromatic rings, which is the reason why the methyl band of toluene is at lower field strength [7] than the corresponding band for methyl*cyclo*hexane, is presumably the factor causing both methyl bands of the acetylquinoxaline (IV; R = Me) to be at lower field strengths than the corresponding bands for the reduction product.

The complete reduction of the ketone (IV; R = Me) was investigated in order to provide chemical confirmation of the dihydroquinoxaline structure for the red reduction product. Over Raney nickel or palladised charcoal, hydrogenation proceeded slowly until the disappearance of the red colour, with the uptake of between three and four mols. of hydrogen. The products could only satisfactorily be identified by benzoylation of the oil thus obtained under Schotten–Baumann conditions followed by chromatography. This yielded an *ON*-dibenzoyl derivative of 1 : 2 : 3 : 4-tetrahydro-2-1′-hydroxyethyl-3-methylquinoxaline (XIV; $R^1 = R^2 = Bz$, $R^3 = H$; or $R^1 = R^3 = Bz$, $R^2 = H$) and 1 : 4-dibenzoyl-2-ethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline (VII; R = Bz). The structure of the latter compound follows from the fact that it is identical with neither the *cis*- nor the *trans*-form of the dibenzoyltetrahydrobenzodiazepine (XV and XVI; R = Bz) which are described below.



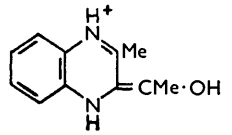
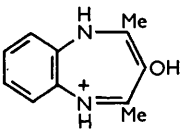
A repetition of this reduction, followed by benzoylation in pyridine, gave a dibenzoyl derivative (VII; R = Bz), the tribenzoyl derivative (XIV; $R^1 = R^2 = R^3 = Bz$), m. p. 205—206°, 2-acetyl-1 : 4-dibenzoyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline (VIII; R = Bz), and a monobenzoyl derivative, which is provisionally assigned the structure (XIV; $R^1 = R^3 = H$, $R^2 = Bz$) since the OH and NH stretching bands in its infrared spectrum were sharp and showed no evidence of hydrogen-bonding. The last compound

[7] Meyer, Saika, and Gutowsky, *J. Amer. Chem. Soc.*, 1953, **75**, 4567.

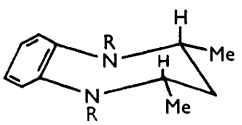
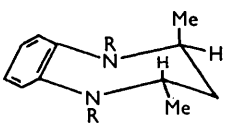
on benzoylation gave another isomer, m. p. 175°, of the tribenzoyl derivative (XIV; $R^1 = R^2 = R^3 = Bz$).

This accumulation of evidence leaves no serious doubt that the red reduction product derived from acetylmethylquinoxaline is anything other than the dihydroquinoxaline (X ⟷ XIII; R = Me). However, with acid, it changes to a purple compound, whose visible spectrum in form, in position, and in intensity ($\lambda_{max.}$ 5400 Å, ε 2300) corresponds approximately to that of dimethylbenzodiazepinium salts (III) ($\lambda_{max.}$ 5100, ε 830) (because of the extremely rapid oxidation of dilute solutions of the reduction product, it was not possible to record its spectrum in the ultraviolet region). This raises the question whether this purple substance has a dihydroquinoxaline structure (XVII) or the alternative 3-hydroxybenzodiazepinium cation structure (XVIII) formed by the reaction sequence (X) ⟶ (V) ⟶ (VI) ⟶ (XVIII) postulated earlier. However, hydrogenation of the ketone (IV; R = Me) under acidic conditions until the purple colour had been discharged led to the same products as had been formed under neutral conditions, (XIV; $R^1 = R^2 = R^3 = H$) and tetrahydroethylmethylquinoxaline (VII; R = H) being isolated as their monobenzoyl derivatives, thus disposing of the seven-membered ring structure.

For comparison, the *cis*- (XV; R = H) and the *trans*-form (XVI; R = H) of tetrahydrodimethylbenzodiazepine were required. They were obtained by hydrogenation of the dimethylbenzodiazepine followed by chromatography and were characterised as their benzoyl derivatives.

(XVII)   (XVIII)

The configurations of these isomers were assigned by examination of the nuclear magnetic resonance spectra of the two dibenzoyl derivatives (XV and XVI; R = Bz) in ethanol-free chloroform. The high molecular weight of these compounds limited the absorptions recorded to the methyl bands, which occurred in the region expected for a methyl group attached to a saturated carbon atom. The higher-melting derivative showed two peaks of equal intensity 6·3 c./sec. apart, and the other, three peaks with a separation of 6·5 c./sec., the centre one being of greatest intensity. Since a methyl band would be split into a doublet

(XIX)   (XX)

by spin–spin interaction with the adjacent CH group, the triplet must arise from the superimposition of two distinct doublets, one band of each being approximately coincident. The triplet splitting of the methyl band by the CH_2 group would be a second-order effect only, the expected magnitude of which would be less than 1 c./sec. This was not resolved and was responsible only for the broadening of each line. In the *cis*-form (XIX) the methyl groups have identical (presumably pseudoequatorial) conformations, but in the *trans*-form (XX) one group is pseudoaxial and thus has a different environment from the other. The *trans*-isomer will therefore produce a triplet absorption, and this configuration may be assigned to the lower-melting derivative and parent compound.

Experimental

Unless otherwise specified, alumina refers to Spence's grade H alumina deactivated with 5% of 10% aqueous acetic acid.

2-Acetyl-1 : 4-dihydro-3-methylquinoxaline.—2-Acetyl-3-methylquinoxaline (0·5 g.) in dry ethanol (50 c.c.) was hydrogentated over 5% palladised charcoal (which had been pre-equilibrated with hydrogen) until one mol. of hydrogen had been absorbed, then filtered from catalyst under nitrogen and evaporated under reduced pressure of nitrogen on a water-bath at 40°. The solid residue was washed with ether under nitrogen and dried *in vacuo*. The *dihydroquinoxaline* formed red-brown needles, m. p. 149—151° (*in vacuo*) (Found: C, 70·1; H, 6·5; N, 14·7. $C_{11}H_{12}ON_2$ requires C, 70·2; H, 6·4; N, 14·9%), $\lambda_{max.}$ 4895 Å in EtOH. The crystals were oxidised in two days in the air to 2-acetyl-3-methylquinoxaline, identified by m. p. and mixed m. p. 86—87° and by its infrared spectrum. Solutions of the reduction product are oxidised very rapidly to the same compound, but acidified solutions are stable for a few hours.

Absorption spectrum (with D.M.R.). 2-Acetyl-3-methylquinoxaline (50 mg.) was dissolved in methanol (400 c.c.) and 48% hydrobromic acid (0·5 c.c.). Hydrogen was bubbled through 4 c.c. portions of this solution contained in a test-tube with a little platinum oxide catalyst. When the developing purple colour was judged visually to have attained its maximum intensity, the solution was decanted from catalyst and the optical density at a preset wavelength was measured on a Unicam spectrophotometer. This sequence of operations was repeated several times at each wavelength, the maximum value being accepted as the optical density at that wavelength. The results, when plotted, fell on a smooth curve with $\lambda_{max.}$ 5400 Å (ε 2300).

2-Acetyl-1 : 4-dihydro-3-phenylquinoxaline.—2-Acetyl-3-phenylquinoxaline [1] (0·5 g.) in ethanol (50 c.c.) was hydrogenated over 5% palladised charcoal (100 mg.) until one mol. of hydrogen had been absorbed, then worked up as above. The *product* was obtained as purple-red needles, m. p. 181—182° (*in vacuo*) (Found: C, 76·8; H, 5·6; N, 11·1. $C_{16}H_{14}ON_2$ requires C, 76·8; H, 5·6; N, 11·2%), ν (in Nujol) 3350, 3250 cm.$^{-1}$, $\lambda_{max.}$ 5130 Å in EtOH. The solution in ethanol was oxidised very rapidly to the starting ketone, identified by m. p., mixed m. p. 111—112°, and infrared spectrum.

Further Reduction of 2-Acetyl-3-methylquinoxaline.—(*a*) 2-Acetyl-3-methylquinoxaline (500 mg.) in ethanol (50 c.c.) with 5% palladised charcoal (200 mg.) absorbed 232 c.c. of hydrogen (3·54 mols.) during 30 hr., the solution becoming colourless. The product, an oil (440 mg.), was shaken with benzoyl chloride and 2N-sodium hydroxide, isolated with ether, and chromatographed on alumina (140 g.) in 1 : 1 benzene–light petroleum. Prisms (15 mg.), m. p. 238—240°, from benzene–light petroleum were obtained, followed by 1- or 4-*benzoyl-2-1′-benzoyloxyethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline* as an oil which was obtained crystalline (50 mg.; m. p. 200—202°) from benzene–light petroleum (Found: C, 75·9; H, 6·1; N, 7·5%; *M*, 405. $C_{25}H_{24}O_3N_2$ requires C, 75·0; H, 6·0; N, 7·0%; *M*, 400), ν (in Nujol) 3340, 1720, 1638 cm.$^{-1}$. Continued elution with the same solvent gave 1 : 4-*dibenzoyl-2-ethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline, isomer A* (110 mg.), m. p. 178—179° (from benzene–light petroleum) (Found: C, 77·9; H, 6·5; N, 6·9. $C_{25}H_{24}O_2N_2$ requires C, 78·1; H, 6·3; N, 7·3%), ν (in Nujol) 1645 cm.$^{-1}$.

(*b*) 2-Acetyl-3-methylquinoxaline (800 mg.) was hydrogenated as in the immediately preceding experiment and benzoylated by boiling it for 40 min. under reflux with benzoyl chloride (0·8 c.c.) and pyridine. Isolation with ether gave an oil, which when washed with benzene (25 c.c.) gave yellow 1-*benzoyl-1 : 2 : 3 : 4-tetrahydro-3-1′-hydroxyethyl-2-methylquinoxaline* (480 mg.), m. p. 188—189° (from aqueous methanol) (Found: C, 72·9; H, 6·6; N, 9·9. $C_{18}H_{20}O_2N_2$ requires C, 73·0; H, 6·8; N, 9·5%), ν (in Nujol) 3440, 3390, 1613 cm.$^{-1}$. The compound is dimorphic, being reversibly converted by crystallisation from benzene into a colourless form, m. p. 196—198°, ν (in Nujol) 3450, 3330, 1600 cm.$^{-1}$. Both forms have the same ultraviolet and infrared absorptions, ν (in $CHCl_3$) 3600, 3440, 1633 cm.$^{-1}$. This monobenzoyl derivative (80 mg.) was boiled for 45 min. in pyridine with benzoyl chloride (1·5 c.c.); the product was isolated with ether and chromatographed on alumina (20 g.) with 1 : 1 benzene–light petroleum, yielding 1 : 4-*dibenzoyl-2-1′-benzoyloxyethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline* (*isomer A*) as an oil which separated from benzene–light petroleum in crystals (60 mg.), m. p. 175° (Found: C, 75·9; H, 5·5; N, 5·4. $C_{32}H_{28}O_4N_2$ requires C, 76·2; H, 5·6; N, 5·6%), ν (in Nujol) 1730 and 1657 cm.$^{-1}$.

The benzene-soluble material was chromatographed on alumina (80 g.). Elution with 1 : 1 benzene–light petroleum gave an orange oil A (110 mg.); further elution with benzene gave an oil B (140 mg.), and 1 : 5 ether–benzene gave an oil C (330 mg.). Washing the column finally with ether gave more 1-benzoyl-1 : 2 : 3 : 4-tetrahydro-3-1′-hydroxyethyl-2-methylquinoxaline (90 mg.), m. p. 188—189°. The oil A was boiled under reflux for 1 hr. with pyridine and benzoyl

chloride (0·5 c.c.); isolation with ether and chromatography on alumina (15 g.) in 1 : 1 benzene–light petroleum gave 2-*acetyl*-1 : 4-*dibenzoyl*-1 : 2 : 3 : 4-*tetrahydro*-3-*methylquinoxaline* (70 mg.), m. p. 116° (from benzene–light petroleum) (Found: C, 74·4; H, 5·6; N, 6·2. $C_{25}H_{22}O_3N_2$ requires C, 75·4; H, 5·6; N, 7·0%), ν (in Nujol) 1690 and 1648 cm.$^{-1}$. Continued development gave 1 : 4-dibenzoyl-2-ethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline (50 mg.), m. p. 178—179° (from benzene–light petroleum). Similar treatment of oil B gave more of this dibenzoyltetrahydroquinoxaline (40 mg.). Oil C, when benzoylated in boiling pyridine with benzoyl chloride (1 c.c.), gave an oil which on crystallisation from benzene–light petroleum gave 1 : 4-*dibenzoyl*-2-1′-*benzoyloxyethyl*-1 : 2 : 3 : 4-*tetrahydro*-3-*methylquinoxaline* (*isomer B*) (290 mg.), m. p. 205—206°, depressed on admixture with isomer A to 160—163° (Found: C, 76·6; H, 5·7; N, 5·3%), ν (in Nujol) 1710, 1660, and 1645 cm.$^{-1}$.

(*c*) 2-Acetyl-3-methylquinoxaline (500 mg.) in ethanol (40 c.c.) and concentrated hydrochloric acid (0·25 c.c.) with 5% palladised charcoal (200 mg.) absorbed hydrogen (227 c.c., 3·60 mols.) during 3 hr. with the discharge of the initial intense purple colour. Benzoylation in boiling pyridine with benzoyl chloride (2 c.c.) followed by chromatography on alumina (150 g.) with 1 : 1 benzene–light petroleum gave 1- or 4-*benzoyl*-2-*ethyl*-1 : 2 : 3 : 4-*tetrahydro*-3-*methylquinoxaline* (210 mg.), m. p. 156—157° (from benzene–light petroleum) (Found: C, 77·1; H, 7·2; N, 9·7. $C_{18}H_{20}ON_2$ requires C, 77·1; H, 7·2; N, 10·0%), ν (in Nujol) 3330 and 1618 cm.$^{-1}$. This compound (200 mg.), heated under reflux for 1 hr. with benzoyl chloride (0·5 c.c.) in pyridine, gave 1 : 4-dibenzoyl-2-ethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline (170 mg.) which separated from benzene–light petroleum with m. p. 178—179°, alone and when mixed with a specimen of the same compound obtained from experiment (*a*) above.

Further elution with ether yielded the above 1-benzoyl-1 : 2 : 3 : 4-tetrahydro-3-1′-hydroxyethyl-2-methylquinoxaline (160 mg.), m. p. 188—189°.

2-1′-*Hydroxyethyl*-3-*methylquinoxaline*.—2-Acetyl-3-methylquinoxaline (0·5 g.) in methanol (25 c.c.) was shaken for 30 min., then boiled under reflux for 30 min., with a solution of potassium borohydride (0·4 g.) in methanol (50 c.c.) and water (25 c.c.). The mixture was acidified with acetic acid (30 c.c.) and water (200 c.c.), then basified. The product, isolated with ether, was chromatographed on alumina (30 g.) in 1 : 1 benzene–light petroleum, giving starting material (70 mg.) followed by 2-1′-*hydroxyethyl*-3-*methylquinoxaline* (270 mg.), m. p. 81° (from ligroin) (Found: C, 69·9; H, 6·3; N, 14·7. $C_{11}H_{12}ON_2$ requires C, 70·2; H, 6·4; N, 14·9%), ν (in Nujol) 3230 cm.$^{-1}$. Benzoylation in pyridine gave 2-1′-*benzoyloxyethyl*-3-*methylquinoxaline*, needles, m. p. 144° (from methanol) (Found: N, 9·9. $C_{18}H_{16}O_2N_2$ requires N, 9·6%).

Reaction of 2-Acetyl-1 : 4-dihydro-3-methylquinoxaline with Phenylhydrazine.—The hydrogenation of 2-acetyl-3-methylquinoxaline (500 mg.) in ethanol (50 c.c.) over palladised charcoal was stopped after the absorption of 1 mol. of hydrogen. Phenylhydrazine (0·54 c.c., 2 mol.) and concentrated hydrochloric acid (0·3 c.c.) were added and the whole was shaken in an atmosphere of nitrogen until the red colour was discharged (3 hr.), then made alkaline and steam-distilled. The distillate gave an oil, which was warmed with cupric sulphate solution to destroy any phenylhydrazine, then treated with aqueous ammonia. Aniline was isolated with ether and identified by conversion into phenylazo-β-naphthol (300 mg.), m. p. and mixed m. p. 133°.

The involatile residue from the steam-distillation was isolated with ether and crystallised from aqueous methanol, giving 2-acetyl-3-methylquinoxaline phenylhydrazone (480 mg.), m. p. 175—176°. Similar results were obtained from a solution which had been filtered from catalyst before treatment with phenylhydrazine.

Decomposition of 2-Acetyl-1 : 4-dihydro-3-methylquinoxaline by Acid.—A solution of 2-acetyl-3-methylquinoxaline (500 mg.) in ethanol (50 c.c.) was hydrogenated over palladised charcoal until one mol. had been absorbed. Then, in the presence of the catalyst, it was treated with deoxygenated water (20 c.c.) and concentrated hydrochloric acid (0·5 c.c.) and boiled under nitrogen until the purple colour disappeared (*ca.* 10 min.). Chromatography of the product on alumina (60 g.) with light petroleum gave two orange oils, A (330 mg.) and B (160 mg.). Benzoylation of oil A in pyridine followed by chromatography on alumina (20 g.) gave 1 : 4-dibenzoyl-2-ethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline, isomer A (15 mg.), m. p. 178—179°, as the only identifiable product. Similar treatment of oil B gave 1 : 4-*dibenzoyl*-2-*ethyl*-1 : 2 : 3 : 4-*tetrahydro*-3-*methylquinoxaline*, *isomer B*, as an oil (100 mg.) which formed crystals (25 mg.), m. p. 183—184° (from benzene–petroleum), mixed m. p. with isomer A, 154—156° (Found: C, 77·9; H, 5·9. $C_{25}H_{24}O_2N_2$ requires C, 78·1; H, 6·3%). A similar decomposition, conducted in the absence of catalyst, gave no identifiable products.

Dismutation of 2-Acetyl-1 : 4-dihydro-3-methylquinoxaline.—The hydrogenation of 2-acetyl-3-methylquinoxaline (1 g.) in ethanol (50 c.c.) over palladised charcoal was stopped after the absorption of one mol., and 20 c.c. of the reduced solution were allowed to reoxidise in air. Chromatography then yielded only starting material. The remainder of the reduced solution was heated under nitrogen, together with the catalyst, until decolorised (3½ hr.), and the product was chromatographed on alumina (18 g.) with light petroleum, 2-acetyl-3-methylquinoxaline (460 mg.) and an oil A (250 mg.) being obtained. Further elution with 1 : 1 benzene–light petroleum gave an oil B (100 mg.).

Chromatography on alumina (50 g.) in 1 : 1 benzene–light petroleum of the product obtained by benzoylating oil A gave 2-1′-benzoyloxy-3-methylquinoxaline (170 mg.), m. p. and mixed m. p. 144° (from methanol), and 2-acetyl-1 : 4-dibenzoyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline as an oil (100 mg.), which formed crystals (40 mg.), m. p. 116°, from benzene–light petroleum. Similar treatment of oil B gave more 2-1′-benzoyloxy-3-methylquinoxaline (105 mg.).

The reduced solution, when heated under nitrogen in the absence of catalyst, was decolorised only very slowly and acetylmethylquinoxaline was the only product isolated.

Reduction of 2 : 4-Dimethyl-1 : 5-benzodiazepine.—(*a*) 2 : 4-Dimethyl-1 : 5-benzodiazepine (1·0 g.) in ethanol (50 c.c.) with 5% palladised charcoal (100 mg.) absorbed hydrogen (283 c.c., 1·03 mol.) during 30 hr. The oily product was benzoylated in 2N-sodium hydroxide and chromatographed on alumina (100 g.) in 2 : 1 benzene–light petroleum, giving 1-*benzoyl*-1 : 2 : 4 : 5-*tetrahydro*-cis-2 : 4-*dimethyl*-1 : 5-*benzodiazepine* (590 mg.), m. p. 156° (from benzene–light petroleum) (Found: C, 77·3; H, 7·2; N, 9·8. $C_{18}H_{20}ON_2$ requires C, 77·1; H, 7·2; N, 10·0%), ν (in Nujol) 3360, 1630 cm.$^{-1}$. Benzoylation of this compound (350 mg.) in pyridine followed by chromatography over alumina (25 g.) in 1 : 1 benzene–light petroleum gave 1 : 5-*dibenzoyl*-1 : 2 : 4 : 5-*tetrahydro*-cis-2 : 4-*dimethyl*-1 : 5-*benzodiazepine* (250 mg.), m. p. 161—162° (from benzene–light petroleum) (Found: C, 78·6; H, 6·3; N, 7·2. $C_{25}H_{24}O_2N_2$ requires C, 78·1; H, 6·3; N, 7·3%), ν (in Nujol) 1640 cm.$^{-1}$.

(*b*) The above hydrogenation was repeated on the dimethylbenzodiazepine (2·5 g.), but the product, without benzoylation, was immediately chromatographed on alumina (150 g.) in light petroleum, giving 1 : 2 : 4 : 5-*tetrahydro*-trans-2 : 4-*dimethyl*-1 : 5-*benzodiazepine*, an oil (350 mg.), b. p. 72—74°/0·075 mm. (Found: C, 74·5; H, 8·9; N, 16·4. $C_{11}H_{16}N_2$ requires C, 75·0; H, 9·1; N, 15·9%), ν (in Nujol) 3330 cm.$^{-1}$. Benzoylation in pyridine gave an oil, which was chromatographed in 1 : 1 benzene–light petroleum on alumina (70 g.), to give 1 : 5-*dibenzoyl*-1 : 2 : 4 : 5-*tetrahydro*-trans-2 : 4-*dimethyl*-1 : 5-*benzodiazepine*, m. p. 129—130° (from benzene–light petroleum) (Found: C, 78·4; H, 6·6; N, 6·9. $C_{25}H_{24}O_2N_2$ requires C, 78·1; H, 6·3; N, 7·3%), ν (in Nujol) 1640 cm.$^{-1}$.

Continued elution of the column with 1 : 5 benzene–light petroleum gave 1 : 2 : 4 : 5-*tetrahydro*-cis-2 : 4-*dimethyl*-1 : 5-*benzodiazepine* (1·64 g.), m. p. 57° (from ligroin) (Found: C, 74·3; H, 9·2; N, 16·0. $C_{11}H_{16}N_2$ requires C, 75·0; H, 9·1; N, 15·9%), ν (in Nujol) 3350 cm.$^{-1}$. Benzoylation in pyridine gave an oil which was chromatographed on alumina. Elution with 1 : 1 benzene–light petroleum gave the monobenzoyl derivative, m. p. 156°. Further elution with benzene gave the dibenzoyl derivative, m. p. 161—162°.

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