692. *Diazepines. Part III.*[1] *Some Benzodiazepines*

By Douglas Lloyd, Ronald H. McDougall, and Donald R. Marshall

A number of 3*H*-1,5-benzodiazepines and related compounds have been prepared, and their properties studied.

Most recorded preparations of 3*H*-1,5-benzodiazepines (I) have made use of the original method of Thiele and Steimmig,[2] namely the condensation of *o*-phenylenediamine with a 1,3-diketone in the presence of ethanolic acetic acid. Their preparation by reaction of the diamine with benzaldehyde or its derivatives has also been described.[3] In the present work, Thiele's method has been used to prepare a series of benzodiazepines from acetylacetone and a variety of substituted diamines. Condensation has also been effected in ethereal solution using dry hydrogen chloride as catalyst. In the latter case the dihydrochloride is formed; addition of water converts this into the monoacid salt. By condensation of *o*-phenylenediamine with 1-ethoxy-1,3,3-trimethoxypropane, salts of the hitherto unknown unsubstituted benzodiazepine have been prepared.

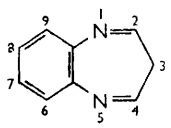
There was sometimes difficulty in obtaining pure samples of substituted *o*-phenylenediamines, especially those having further electron-releasing groups present. To overcome this, a modified procedure was used in which an *o*-nitro-amine was reduced by means of hydrazine hydrate in the presence of Raney nickel;[4] immediately after decomposition of the excess of hydrazine hydrate the resultant solution was filtered directly into a solution

[1] Part II, D. Lloyd and D. R. Marshall, *J.*, 1958, 118.
[2] J. Thiele and G. Steimmig, *Ber.*, 1907, **40**, 955.
[3] S. Weil and H. Marcinkowska, *Roczniki Chem.*, 1934, **14**, 1312; N. V. Subba Rao and C. V. Ratnam, *Current Sci.*, 1955, **24**, 299.
[4] D. Balcom and A. Furst, *J. Amer. Chem. Soc.*, 1953, **75**, 4334.

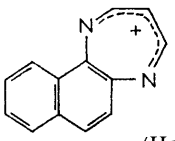
of the diketone. The diamine is protected from oxidation throughout its preparation by the excess of hydrazine present.

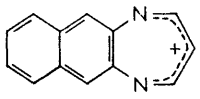
An attempt to prepare an ethyl benzodiazepine-6-carboxylate by condensation of ethyl diacetoacetate with *o*-phenylenediamine gave only 2-methylbenzimidazole (cf. ref. 14).

The reaction of 2,3-diaminonaphthalene with acetylacetone in methanolic acetic acid, followed by the addition of concentrated hydrochloric acid, has been reported [5] to give a purple hydrochloride which, on treatment overnight with sodium hydroxide, gave a base. The structure (III) was assigned to the base and the hydrochloride was assumed to have the corresponding protonated structure. This hydrochloride has been re-examined in the



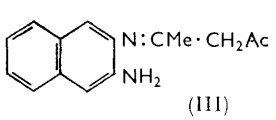
(I)


(IIa)

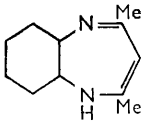

(IIb)

present work. In view of its colour and the shape of its ultraviolet (u.v.) spectrum, which is similar to that of other benzodiazepinium salts but with the u.v. peaks shifted to longer wavelengths (see Figure 1), it seems probable that it is in fact a hydrated naphthodiazepinium salt. (Other hydrates of benzodiazepinium salts are recorded.[6]) The u.v. spectra of 1,5-benzodiazepinium and naphtho[1,2-*b*]- (IIa) and naphtho[2,3-*b*]-[1,4]diazepinium salts (IIb) bear a relationship which parallels the relationship between the spectra of naphthalene, anthracene, and phenanthrene. The corresponding naphtho[1,2-*b*][1,4]diazepinium salt was readily prepared from 1-nitro-2-naphthylamine, whilst benzoylacetone and dibenzoylmethane both react with 2,3-diaminonaphthalene to give naphthodiazepinium salts on addition of hydrochloric acid, although, in the absence of hydrochloric acid, anils corresponding to (III) are produced.[5] It thus seems most likely that the hydrochloride is a naphthodiazepinium salt but that if it is set aside with alkali for a number of hours, the seven-membered ring is opened to give the anil (III). It is known that the condensation reactions leading to diazepine formation involve equilibria which are very unfavourable in strongly alkaline solution (see below and ref. 7) so that ring-opening under these conditions is likely.

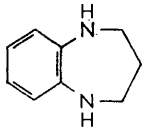
Attempts were also made to prepare 1,5-benzodiazepines by dehydrogenation of 5a,6,7,8,9,9a-hexahydro-2,4-dimethyl-1*H*-1,5-benzodiazepine (IV) and of 2,3,4,5-tetrahydro-1*H*-1,5-benzodiazepine (V), but the desired products were not obtained.



(III)



(IV)

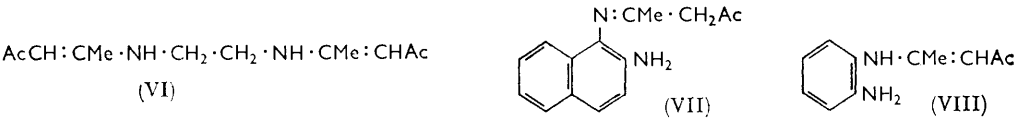


(V)

The condensation between *o*-phenylenediamine and acetylacetone is pH-dependent,[7] as is that between non-benzenoid amines and acetylacetone.[8] In the latter case, at pH values between 6 and 10, an alternative product is formed, which has been shown to have the extended amide structure (VI).[9] A monoanil, to which structure (VII) was assigned, has been obtained from the reaction of benzoylacetone with 1,2-diaminonaphthalene, which yields the diazepine under more vigorous conditions.[10] No such anil has been reported

[5] W. Ried and E. Torinus, *Chem. Ber.*, 1959, **92**, 2902.
[6] J. A. Barltrop, C. G. Richards, D. M. Russell, and G. Ryback, *J.*, 1959, 1132.
[7] C. A. C. Haley and P. Maitland, *J.*, 1951, 3155.
[8] D. Lloyd and D. R. Marshall, *J.*, 1956, 2597.
[9] D. Lloyd, R. H. McDougall, and D. R. Marshall, unpublished work.
[10] W. Ried and W. Höhne, *Chem. Ber.*, 1954, **87**, 1801.

from the reaction of *o*-phenylenediamine with acetylacetone, and this reaction was therefore re-examined.



Buffered aqueous solutions of the reagents were kept at 17° for 24 hours, and alkali was then added to precipitate the diazepine base. (It was established that this addition did not affect the final yield.) The results are shown in Table 1.

TABLE 1

Initial pH of buffer soln.	4·0	5·4	6·0	6·8	7·5	9·6
Yield of product (%)	60·3	57·0	39·1	45·0	48·0	31·9
M. p. of product (lit.,[2] 132°) ...	125—126°	92—100°	*	*ca.* 115°	127—130°	130—131°

* Crystals too soft and sticky for m. p. determination.

It is clear that the product at pH values *ca.* 6 is impure. The impurity is most unlikely to be *o*-phenylenediamine, as these pH values are close to that (6·8) at which condensation of *o*-phenylenediamine with acetylacetone should theoretically proceed to the greatest extent. The most likely impurity is a monoanil.

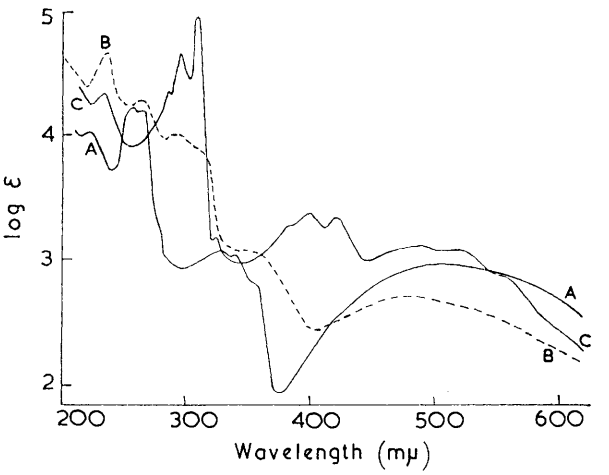
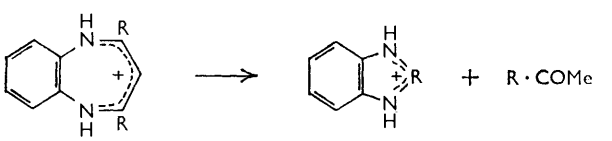


FIGURE 1. Absorption spectra of naphthalodiazepinium salts:
A, 2,4-dimethyl-1,5-benzodiazepinium chloride
B, 2,4-dimethylnaphtho[1,2-*b*][1,4]diazepinium chloride
C, 2,4-dimethylnaphtho[2,3-*b*][1,4]diazepinium chloride

It was not possible to isolate this product in a pure state but an impure sample, separated chromatographically under conditions unlikely to lead to decomposition of the diazepine, had an infrared (i.r.) spectrum consistent with structure (VIII). Such an anil is likely to be most stable in nearly neutral solutions (cf. ref. 8).

Decomposition of Benzodiazepines.—It is known [2] that, on being heated with water, benzodiazepinium salts decompose to benzimidazoles and ketones:



Both the salts and the free bases decompose on standing in aqueous solution at room temperature. The u.v. spectra of the solutions change after a few hours and eventually become those of benzimidazoles. In either case, ring-opening may actually involve the free base; this is suggested by the fact that the presence of a trace of mineral acid greatly

retards the reaction. Methanolic solutions are also more stable; weakly acidic methanolic solutions are completely stable for at least two weeks.

A similar change can be brought about by the dry distillation of benzodiazepinium salts. Since a ketone is also formed it seems likely that ring-opening must involve either water of crystallisation or adsorbed water. It is possible that some of the quoted melting points of benzodiazepinium salts are in fact those of the benzimidazole salts, interconversion having taken place at a lower temperature.

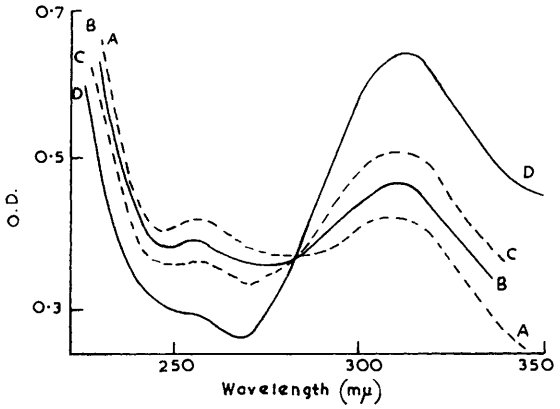
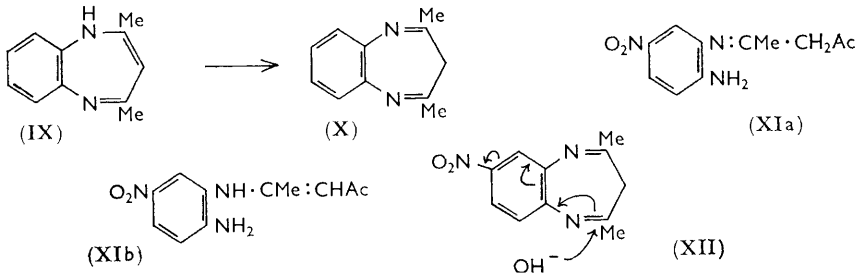


FIGURE 2. Decomposition of 2,4-dimethyl-7-nitro-3*H*-1,5-benzodiazepine in alkali:

A, initial spectrum
B, after 5 min.
C, after 10 min.
D, after 24 hr.

A different type of decomposition occurs when 2,4-dimethyl-7-nitro-3*H*-1,5-benzodiazepine is dissolved in methanolic alkali. The spectrum changes slowly, as shown in Figure 2. Acidification at any stage regenerates the benzodiazepinium cation. Figure 2 shows a good isosbestic point, indicating that only two species are involved, the diazepine



base and the product. This is unlikely to be a tautomeric change of the type (IX) ⟶ (X), which has previously been noted,[11] owing to the relative slowness at which it proceeds and the bathochromic shift which is involved. The spectrum of the product excludes the possibility that complete hydrolysis to the diamine and acetylacetone has occurred; it resembles that of acetylacetone monoanil and the product is therefore probably the monoanil (XIa) or its tautomer (XIb) formed by nucleophilic attack at the 7-carbon atom [see (XII)]. When the aqueous solution of this 7-nitrobenzodiazepine is boiled and cooled, 4-nitro-1,2-diaminobenzene separates out. The presence of other electron-withdrawing substituents in the 7-position (*e.g.*, carboxyl) also appears to increase the ease of hydrolysis of benzodiazepines, and in these cases too diamines are obtained rather than benzimidazoles.

Substitution Reactions.—The action of one molar equivalent of bromine on 2,4-dimethyl-3*H*-1,5-benzodiazepine gave variable and unreproducible results. Treatment of the benzodiazepinium bromide or perchlorate with six molar equivalents of bromine produced dark blue crystals, the elementary analysis and u.v. spectrum of which suggested

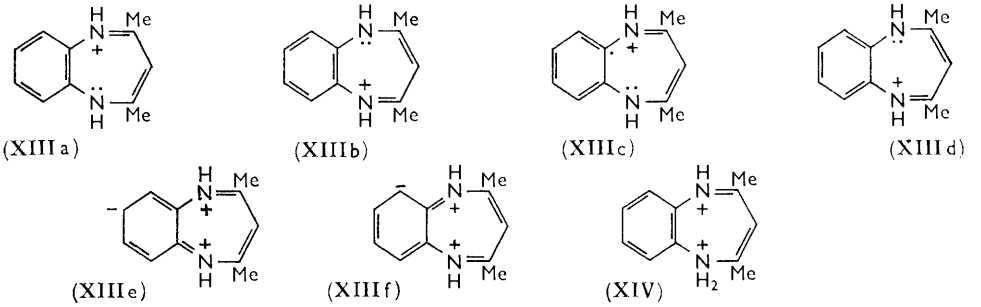
[11] G. Schwarzenbach and K. Lütz, *Helv. Chim. Acta*, 1940, **23**, 1147.

them to be the 6,7,8,9-tetrabromo-1,5-benzodiazepinium bromide. *N*-Bromosuccinimide, which reacts with 2,3-dihydro-1,4-diazepines in the 6-position,[1] gave no identifiable product.

Attempted nitration of the base with copper nitrate or urea nitrate gave only tars. It is likely that oxidation took place; the base is fairly quickly oxidised on exposure to air. Sodamide in boiling xylene did not react with the base.

Reduction.—Catalytic reduction of 3*H*-1,5-benzodiazepines has previously been recorded.[5,10,12] After 2,4-dimethyl-3*H*-1,5-benzodiazepine had been refluxed with lithium aluminium hydride in tetrahydrofuran it was recovered unchanged. Sodium in ethanol produced a tar from which no tractable products could be obtained.

Spectra, Basicity, and Structure.—The 3*H*-1,5-benzodiazepine bases have been shown to have the dianil type of structure (X).[6,13] The monoacid salts have intense purple colours and it seems certain that a tautomeric shift to structure (XIII) must take place during



or after protonation. Resonance canonical formulæ such as (XIIIa—d) can then be written for this cation. This conjugated system, involving both rings, accounts for the broad maxima at *ca.* 500 mμ in the spectra of benzodiazepinium salts. Higher-energy forms such as (XIIIe and f) may also contribute and may explain the ready electrophilic substitution by bromine at each of the four free positions of the benzene ring to give a tetrabromo-derivative. In the doubly charged benzodiazepinium cation (XIV) which is formed in concentrated acids ($pK_1 \sim -1$), conjugation is interrupted by the R–$\overset{+}{N}H_2$–R group and this ion is colourless. The u.v. spectrum has a peak at 260 mμ, which accords with the assigned structure (cf. 1,2-benzocyclohepta-1,3,5-triene, $\lambda_{max.}$ 277 mμ).[14]

1,5-Benzodiazepines with various substituent groups in the 7′-position of the benzene ring all have similar u.v. spectra but the peaks are shifted to longer wavelengths. In the visible portion of the spectra, substitution of methyl, chlorine, carboxy-, nitro-, and thiomethoxy-groups at the 7-position caused a bathochromic shift, whereas methoxy- and bis-1,2-ethylenedioxy-groups caused a hypsochromic shift.

In contrast to the 2,3-dihydro-1,4-diazepines (5,7-dimethyl, pK_2 13·4), the 1,5-benzodiazepines are weaker bases (2,4-dimethyl, pK_2 8·99). They also form doubly charged cations ($pK_1 \sim -1$) in weaker acid than is required to form the dication of the dihydrodiazepine ($pK_1 \sim -3$). This is consistent with there being electronic interaction between the two rings. Electron-withdrawing groups at the 7-position further lower the basicity.

Several factors may contribute to the lower basicity of benzodiazepines, compared with that of the corresponding dihydrodiazepines. In the case of the latter the conjugated structure (IV) is more stable than the isomeric di-imine structure.[9] In contrast, the dianil form (X) of benzodiazepines is more stable than the conjugated form (IX). Salt formation from benzodiazepines thus involves tautomeric change to the less-stable form and is energetically less favoured in consequence.

[12] J. A. Barltrop, C. G. Richards, and D. M. Russell, *J.*, 1959, 1423.
[13] I. L. Finar, *J.*, 1958, 4094.
[14] G. Wittig, H. Eggers, and P. Duffner, *Annalen*, 1958, **619**, 10.

This low basicity in turn explains the ready hydrolysis and ring-contraction of benzodiazepines in neutral solution for, except in strongly acid conditions (under which benzodiazepines are more stable), there will aways be present a significant concentration of the (dianil) base.

If the cation (or the conjugated form of the base) possessed any marked aromatic stability, the equilibria involved would be expected to favour their formation. Although the weak basicity and instability of benzodiazepines do not necessarily show aromatic character to be totally lacking in the seven-membered ring of the cation, it must be concluded that any aromatic stability cannot be great. This is in agreement with the fact that the cation (and the conjugated form of the base) involve 12 π-electrons (or 8, if the seven-membered ring alone is considered) and thus do not satisfy the requirements of Hückel's rule.

Experimental

Preparation of 3H-1,5-*Benzodiazepines by Thiele's Method.*[1]—*o*-Phenylenediamine (1·08 g., purified by vacuum sublimation), acetylacetone (1·0 ml.), glacial acetic acid (1·0 ml.), and ethanol (10 ml.) were refluxed for 2 min. After the mixture had cooled, concentrated hydrochloric acid (5 ml.) was added and the whole stood overnight at 0°. The precipitated 2,4-dimethyl-1,5-benzodiazepinium chloride (1·80 g., 87%) was filtered off, washed with ethanol and ether, and dried, m. p. 200—201°. The bromide, m. p. 216°, and perchlorate, m. p. 204—205°, were prepared similarly.

The same method was used to obtain 2,4-*dimethyl*-7-*nitro*-1,5-*benzodiazepinium chloride* (83·5%), m. p. 200—202° (Found: Cl, 13·7; N, 16·3. $C_{11}H_{12}ClN_3O_2$ requires Cl, 14·0; N, 16·55%) and nitrate, m. p. 147°; 7-*chloro*-2,4-*dimethyl*-1,5-*benzodiazepinium perchlorate* (41%), m. p. 187—188° (Found: Cl, 23·95; N, 9·5. $C_{11}H_{12}Cl_2N_2O_4$ requires Cl, 23·15; N, 9·1%) and *chloroplatinate* (54·5%), m. p. 180—185° on rapid heating (230° when heated slowly) (Found: Cl, 34·6; N, 6·7. $C_{22}H_{24}Cl_8N_4Pt$ requires Cl, 34·5; N, 6·8%); 7-carboxy-2,4-dimethyl-1,5-benzodiazepinium perchlorate (50·7%), m. p. 243—244°; 2,4-*dimethyl*-7-*methylthio*-1,5-*benzodiazepinium chloride* (50·8%), m. p. 199—200° (Found: Cl, 14·3; N, 11·3; S, 12·8. $C_{12}H_{15}ClN_2S$ requires Cl, 13·95; N, 11·0; S, 12·55%). Mixed sulphates–hydrogen sulphates of 7-methoxy- and 7,7-ethylenedioxy-2,4-dimethyl-3*H*-1,5-benzodiazepines were also prepared.

Preparation of 3H-1,5-*Benzodiazepines in Ether Solution.*—*o*-Phenylenediamine (1·08 g.) was dissolved in ether (100 ml.) and 1-methoxyacetylacetone (1·0 ml.) added. Hydrogen chloride gas was passed through the solution. A white precipitate of the benzodiazepinium dihydrochloride formed, which turned blue on addition of water. 2-Methoxymethyl-4-methyl-1,5-benzodiazepinium chloride was purified by solution in ethanol and reprecipitation with ether (0·55 g., 30%), m. p. 185—188°.

Condensation of o-*Phenylenediamine and* 1-*Ethoxy*-1,3,3-*trimethoxypropane.*—(*a*) *o*-Phenylenediamine (1·08 g.), 1-ethoxy-1,3,3-trimethoxypropane (1·8 g.), glacial acetic acid (1·0 ml.), and ethanol (10 ml.) were refluxed for 2½ min., cooled, and concentrated hydrochloric acid was added. After the mixture had stood overnight at 0°, the purple 1,5-*benzodiazepinium chloride* was filtered off and washed with ethanol and ether (1·59 g., 80%), m. p. 196·5° (Found: Cl, 17·6; N, 14·15. $C_9H_9ClN_2,H_2O$ requires Cl, 17·9; N, 14·1%). The *bromide* was prepared similarly, m. p. 187—189° (Found: N, 10·8. $C_9H_9BrN_2,2H_2O$ requires N, 10·7%).

(*b*) Perchloric acid (60%, 2·7 ml.) in methanol (30 ml.) was added to 1-ethoxy-1,3,3-trimethoxypropane (2·4 g.) and *o*-phenylenediamine (1·5 g.) in methanol (10 ml.). After the mixture had stood for 24 hr. the residue was triturated and rubbed with water. The red 1,5-*benzodiazepinium perchlorate* was filtered and washed with acetone–ether (3·0 g., 82·4%), m. p. 192—196° (Found: Cl, 12·9; N, 10·6. $C_9H_9ClN_2O_4H_2O$ requires Cl, 13·5; N, 10·7%).

Preparation of 1,5-*Benzodiazepines from Nitro-amines.*—Small portions of Raney nickel (W-4) were added to a warm mixture of 4-amino-3-nitrobenzoic acid (0·5 g.), ethanol (20 ml.), and hydrazine hydrate (0·5 ml.) until the solution had become almost colourless. The excess of hydrazine was then decomposed by addition of further Raney nickel, and the solution boiled to expel gases and filtered into acetylacetone (0·35 ml.) in acetic acid (0·3 ml.). The resultant mixture was boiled for 2 min., cooled, and perchloric acid (60%; 5 ml.) added. After the mixture had stood overnight at 0° the precipitate of 7-*carboxy*-2,4-*dimethyl*-1,5-*benzodiazepinium*

perchlorate was filtered off (0·48 g., 55·2%), m. p. 242—243° (Found: Cl, 11·4; N, 8·9. $C_{12}H_{13}ClN_2O_6$ requires Cl, 11·2; N, 8·85%). 2,4-*Dimethylnaphtho*[1,2-*b*][1,4]*diazepinium perchlorate* was prepared similarly (80%), m. p. 223—234° (Found: Cl, 11·45; N, 8·95. $C_{15}H_{15}ClN_2O_4$ requires Cl, 11·0; N, 8·7%), as was 2,4,7-trimethyl-1,5-benzodiazepinium perchlorate, m. p. 197—198°.

Reaction of o-*Phenylenediamine with Ethyl Diacetoacetate.*—*o*-Phenylenediamine (0·353 g.) ethyl diacetoacetate (0·562 g.), acetic acid (0·3 ml.), and ethanol (3 ml.) were boiled together for 2 min., cooled, and perchloric acid (60%, 2 ml.) added. After the mixture had stood overnight, pink crystals of 2-methylbenzimidazole perchlorate (0·25 g.) separated, m. p. 163—164° (after washing with ether), mixed m. p. 164—165°.

Condensation of 2,3-*Diaminonaphthalene with Acetylacetone.*—The method of Thiele (see above) gave purple crystals (79·1%), m. p. 256—260° (Found: Cl, 13·1; N, 11·1. $C_{15}H_{15}ClN_2,H_2O$ requires Cl, 12·8; N, 10·15%).

Attempted Dehydrogenation of 5a,6,7,8,9,9a-*Hexahydro*-3H-1,5-*benzodiazepine.*—(i) The diazepine obtained by condensing 1,2-diaminocyclohexane with acetylacetone (cf. ref. 8) was passed in a slow stream of nitrogen over 20% palladium–charcoal at 320°. (ii) A mixture of diazepine and excess of chloranil dissolved in butanol was refluxed for 5 hr. In neither case was any purple product obtained on acidification with hydrochloric acid.

Attempted Dehydrogenation of 2,3,4,5-*Tetrahydro*-1*H*-1,5-*benzodiazepine.*[15]—Neither by passing the tetrahydrobenzodiazepine over palladium–charcoal at 320° nor by refluxing it with chloranil in xylene could a product be obtained corresponding in properties to a 2,3-benzo-1,4-diazepine.

Condensations of o-Phenylenediamine with Acetylacetone in Solutions at Different pH Values.—Solutions of *o*-phenylenediamine (4·3 g. 0·04 mole, purified by vacuum sublimation) and acetylacetone, (4·2 ml., 0·041 mole) in appropriate buffer solutions (280 ml. made up from potassium hydroxide and potassium dihydrogen phosphate) were set aside for 1 or 3 days. 2N-Sodium hydroxide was then added to precipitate the benzodiazepine base.

Attempted Isolation of an Alternative Product in this Condensation.—Mixtures of the reactants which had stood at pH ~6 for 24 hr. were filtered and the products dissolved in benzene and chromatographed on an alumina column, methanol–benzene being used as eluant. Two components separated, the benzodiazepine and a sticky product which could not be purified satisfactorily, but the i.r. spectrum of which was consistent with its having structure (VIII).

Thermal Decomposition of Benzodiazepinium Salts.—A sample of the benzodiazepinium salt was heated in a metal-bath. Acetone distilled off and was characterised (DNP). The residue was extracted with boiling water, filtered, concentrated, and treated with 2N-sodium hydroxide. The benzimidazole base was precipitated and recrystallised from water. The identities of the benzimidazoles were confirmed by mixed m. p. determinations. In this way the following decompositions of 1,5-benzodiazepinium salts were carried out: 2,4-dimethylbenzodiazepinium chloride ⟶ 2-methylbenzimidazole (m. p. 175—176°); 2,4-dimethyl-7-nitrobenzodiazepinium chloride ⟶ 2-methyl-5-nitrobenzimidazole (m. p. 211—212°); 2,4,7-trimethylbenzodiazepinium perchlorate ⟶ 2,5-dimethylbenzimidazole (m. p. 198—199°); 2,4-dimethylnaphtho[1,2-*b*][1,4]diazepinium chloride ⟶ 2-methyl-3*H*-naphth[1,2-*d*]imidazole (picrate m. p. 253—254°); 2,4-dimethylnaphtho[2,3-*b*][1,4]diazepinium chloride ⟶ 2-methyl-1*H*-naphth[2,3-*d*]imidazole (m. p. 283—284°). In general, the chlorides decomposed smoothly but the perchlorates decomposed violently.

Decomposition of 2,4-*Dimethyl*-7-*nitro*-3H-1,5-*benzo*-1,4-*diazepine in Alkali.*—Methanolic sodium hydroxide was added to a solution of the diazepinium salt, the pH of the resultant mixture being 13. The spectrum was recorded at intervals (Figure 2). On acidification after any period the spectrum reverted to that of the original cation. When a solution of this diazepine in 2N-aqueous sodium hydroxide was boiled, orange crystals of 1,2-diamino-4-nitrobenzene separated out, m. p. and mixed m. p. 199—200°.

Bromination of 2,4-*Dimethyl*-3H-1,5-*benzodiazepine and its Perchlorate.*—(*a*) The diazepinium perchlorate (2 g.) (or bromide) was dissolved in glacial acetic acid (1500 ml.) and bromine (2·4 ml.; 6 molar Equiv.) added dropwise with swirling. After 24 hr., dark blue crystals of 6,7,8,9-*tetrabromo*-2,4-*dimethyl*-1,5-*benzodiazepinium bromide* separated out (2·77 g., 80·5%), m. p. 360° (Found: C, 24·35; H, 1·85; N, 5·05. $C_{11}H_9Br_5N_2$ requires C, 23·2; H, 1·6; N, 4·9%).

(*b*) The diazepine base (0·5 g.) was refluxed with *N*-bromosuccinimide (0·518 g.) in carbon

[15] H. Stetter, *Chem. Ber.*, 1953, **86**, 197.

tetrachloride (30 ml.), cooled, and filtered. On removal of the solvent the product decomposed violently, leaving a black residue. Methylene chloride extracted 2,4-dimethyl-1,5-benzodiazepinium bromide, m. p. and mixed m. p. 216—217°, from this residue; no tractable product could be obtained by chromatography or recrystallisation of the black remainder, which melted *ca.* 90° and contained bromine.

Attempted Nitration of 2,4-*Dimethyl*-3H-1,5-*benzodiazepine*.[16]—(*a*) The diazepine (0·5 g.) in acetic anhydride was cooled in acetone–solid carbon dioxide, and a suspension of copper nitrate (0·73 g.) in acetic anhydride (40 ml.) added, with stirring, over 30 min. After a further 60 min., the solution was allowed to reach room temperature and basified with 2N-aqueous potassium hydroxide. Both a methylene chloride extract and the aqueous residue gave only tars.

(*b*) An acetone solution of the diazepine (0·5 g.) and a large excess of urea nitrate was cooled as in (*a*), stirred for 2 hr., and basified with concentrated aqueous sodium hydroxide. The acetone layer was separated, the solvent removed, and the residue dissolved in chloroform and chromatographed on alumina. No tractable products were obtained.

Attempted Reaction of 2,4-*Dimethyl*-3H-1,5-*benzodiazepine with Sodamide*.—A solution of the diazepine (0·5 g.) and sodamide (0·5 g.) in dry xylene (40 ml.) was refluxed under nitrogen for 1 hr. On addition of water, followed by concentrated hydrochloric acid, the hydrochloride of the original diazepine precipitated.

Attempted Reduction of 2,4-*Dimethyl*-3H-1,5-*benzodiazepine*.—(*a*) The diazepine (1 g.) was mixed with lithium aluminium hydride (0·25 g.) in tetrahydrofuran (55 ml.). After addition of water and potassium sodium tartrate solution the mixture was extracted with benzene. Removal of this solvent left the original diazepine (0·59 g.).

(*b*) To the diazepine (1 g.) in ethanol (100 ml.) sodium (5·5 g.) was added over 30 min. After removal of some of the ethanol by distillation, water was added and the solution extracted with ether. A brown oily residue was obtained from which no definite product could be isolated. This residue gave no purple colour with acid and contained no unchanged starting material.

Infrared Spectra.—2,4-Dimethyl-1,5-benzodiazepinium salts had i.r. peaks at 3·03, 3·09, 3·17, 6·14, 6·26, 6·43, 6·60, 7·00, 7·83, 8·03, 8·56, 10·75 μ. Similar peaks were present in the i.r. spectra of the corresponding 7-carboxy-, 7-chloro-, 7-methyl-, and 7-nitro-1,5-benzodiazepinium salts, and 2,4-dimethylnaphtho[1,2-*b*][1,4]diazepinium salts.

Ultraviolet and Visible Spectra.—7-Substituted 2,4-dimethyl-1,5-benzodiazepinium salts in ~0·01N-hydrochloric acid–methanol gave the following values:

7-Substituent	λ (mμ)	log ε	λ (mμ)	log ε	λ (mμ)	log ε	λ (mμ)	log ε
H	224	4·01	260, 269	4·21, 4·19	325, 339	3·06, 3·04	510	2·93
Me	230	3·89	267, 276	4·39, 4·36	335, 343	3·03, 3·05	525	2·82
MeO	229	3·87	270, 286	4·18, 4·18	340, 347	3·30, 3·31	497	3·04
Cl	237	4·24	268, 277	4·54, 4·52	332, 343	2·99, 2·96	516	2·97
CO_2H	246	4·37	280	4·49	333, 345 *	3·07, 3·04	526	2·96
NO_2	260	4·29	309	4·05	350 *	3·55	515	2·86
MeS	227	3·97	270, 278, 309	4·08, 4·08, 3·86	364	3·36	541	2·57
$-OCH_2{\cdot}CH_2O-$	230	3·87	272, 290	4·19, 4·18	337, 346	3·27, 3·28	505	2·85

* Shoulder.

Other diazepinium salts. 6,7,8,9-Tetrabromo-2,3-dimethyl-1,5-benzodiazepinium salts: $\lambda_{max.}$ 208, 227, 272, *ca.* 330sh, *ca.* 550 mμ (log ε 4·27, 4·23, 4·14, 3·66, 2·63); 2,4-dimethylnaphtho-[1,2-*b*][1,5]diazepinium salts; $\lambda_{max.}$ 236, 264, 293, 351, *ca.* 477 mμ (log ε 4·66, 4·28, 4·02, 3·06, 2·67); 2,4-dimethylnaphtho[2,3-*b*][1,4]diazepinium salts: $\lambda_{max.}$ 234, 288, 298, 310, 323, 392sh, 400, 420, 482, 518, 560sh mμ (log ε 4·33, 4·34, 4·67, 4·96, 3·18, 3·24, 3·38, 3·34, 3·10, 3·06, 2·83).

We are indebted to the D.S.I.R. for a research grant (to R. H. McD.), to Ciba–Clayton Ltd. and Imperial Chemical Industries Limited (Dyestuffs Division) for gifts of materials, and to Dr. R. Foster (Queen's College, Dundee) for assistance in recording the u.v. spectra.

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University of St. Andrews. [*Received, June 1st*, 1964.]

[16] Cf. (*a*) A. G. Anderson, jun., J. A. Nelson, and J. J. Tazuma, *J. Amer. Chem. Soc.*, 1953, **75**, 4980; (*b*) W. Treibs, *Angew. Chem.*, 1955, **67**, 76.