Diazepines. Part XI.[1] 6-Halogeno-2,3-dihydro-1*H*-1,4-diazepines

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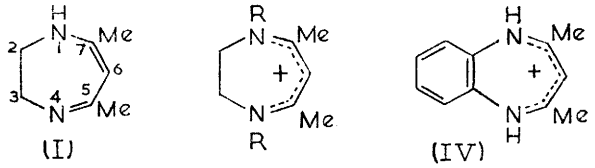
2,3-Dihydro-1*H*-1,4-diazepines are normally brominated at the 6-position. Phenyl substituents are usually unaffected, although with 2,3-dihydro-1,4-diphenyl-5,7-dimethyl-1*H*-1,4-diazepinium salts, the benzene rings are also brominated. 2,3-Dihydro-1,7-dimethyl-5-phenyl-1*H*-1,4-diazepine is brominated at the 7-methyl group. *N*-Chlorosuccinimide and *N*-iodosuccinimide also substitute dihydrodiazepines at the 6-position. Under appropriate conditions 6,6-dihalogenodihydro-6*H*-diazepines have been isolated, but they revert to monohalogeno-compounds in dilute hydrobromic acid. 6-Bromodihydro-1*H*-diazepinium salts are debrominated by strong acid in the presence of bromide ion.

With nucleophiles, 6-bromodihydro-1*H*-diazepines either undergo normal nucleophilic substitution or suffer replacement of the bromine by hydrogen.

THE most characteristic feature of the chemistry of the 2,3-dihydro-1*H*-1,4-diazepinium cations is the readiness with which they undergo electrophilic substitution at the 6-position, with retention of the initial mesomeric system.[2,3] Because of this behaviour they have been described as quasi-aromatic compounds.[3,4] A study has now been made of the halogenation of these compounds, and of the properties of the halogenated derivatives

Bromination of 2,3-*Dihydro*-1H-1,4-*diazepines*.—It has has been shown that 2,3-dihydro-5,7-dimethyl-1*H*-1,4-diazepine (I) and its cation (II) are brominated by



(I) (II) R = H (III) R = Ph (IV)

bromine in organic solvents to give the 6-bromo-product; the same product was obtained by the action of *N*-bromosuccinimide on the cation.[5] Similar reactions occurred when the 2,3-cyclopentano-derivative of (I)[5] and the *NN'*-diphenyldihydrodiazepinium cation (III)[6] were treated with bromine, but the benzodiazepinium cation (IV) underwent bromination in the benzene ring and not in the diazepine ring.[7] Kinetic studies have demonstrated that bromination of (I) in aqueous perchloric acid proceeds by a bimolecular reaction between the cation and bromine.[8]

To establish the generality of this reaction a variety of other 2,3-dihydro-1*H*-1,4-diazepines have been brominated by the reaction of bromine with either the dihydrodiazepine base or its cation, normally in methanol as solvent. By this means the 6-bromo-derivatives of 1,5,7-trimethyl-, 2,5,7-trimethyl-, 2,2,5,7-tetramethyl-, 1,7-dimethyl-5-phenyl-, 1-methyl-5,7-diphenyl-, 5-methyl-7-phenyl-, 5,7-diphenyl and 5-*p*-nitrophenyl-7-phenyl-2,3-dihydro-1*H*-1,4-diazepines have been prepared. That bromination has occurred at the 6-position is shown by the absence of the signal due to the methine proton in the n.m.r. spectra.

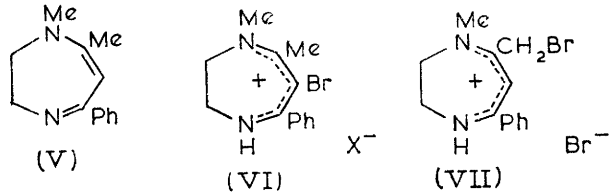
In the above cases, exclusively monobromination resulted and there was no evidence of any bromination in the benzene rings of phenyl substituted compounds. Even when the 5,7-diphenyl derivative was treated with a seven-fold excess of bromine, no polybromination was noted.

The sole exception was provided by the 5,7-dimethyl-1,4-diphenyl cation (III). Although earlier work had shown that this cation could be monobrominated at the 6-position [6] [this has been confirmed by its n.m.r. spectrum: (CF_3CO_2H) 2·5, 5·6, 7·35 (10 : 4 : 6)] the present work showed that, under most conditions, competitive bromination also took place in the phenyl groups, as demonstrated by the n.m.r. and u.v. spectra of the products. When the perchlorate of (III) was treated with one equivalent of bromine, the product, although containing bromine, did not show the bathochromic shift characteristic of 6-brominated dihydrodiazepines [5,6] ($\lambda_{max.}$ 349 mμ; *cf.* $\lambda_{max.}$ (III) 347 mμ); when larger amounts of bromine were used this shift was observed, *e.g.* for 2·5 equivalents of bromine $\lambda_{max.}$ (product) = 376 mμ. When 7 equivalents of bromine were used elemental analysis suggested that mixtures of tri- and tetra-brominated products were obtained. Hydrolysis of the product gave a mixture of brominated dianilinoethanes; the major constituent was bis(2,4-dibromoanilino)ethane. The greater susceptibility to attack of phenyl groups at positions 1 or 4 compared to phenyl groups at positions 5 or 7 is not surprising since the latter sites in the ring are less nucleophilic than positions 1 and 4.

In one instance bromination of a 5-methyl group took place preferentially to substitution at the 6-position.

[1] Part X, A. M. Gorringe, D. Lloyd, and D. R. Marshall, *J. Chem. Soc.* (*C*), 1969, 1081.
[2] A. M. Gorringe, D. Lloyd, D. R. Marshall, and L. A. Mulligan, *Chem. and Ind.*, 1968, 130.
[3] D. Lloyd and D. R. Marshall, *Chem. and Ind.*, 1964, 1760.
[4] A. M. Gorringe, D. Lloyd, and D. R. Marshall, *Chem. and Ind.*, 1968, 1160.
[5] D. Lloyd and D. R. Marshall, *J. Chem. Soc.*, 1958, 118.
[6] C. Barnett, H. P. Cleghorn, G. E. Cross, D. Lloyd, and D. R. Marshall, *J. Chem. Soc.* (*C*), 1966, 92.
[7] D. Lloyd, R. H. McDougall, and D. R. Marshall, *J. Chem. Soc.*, 1965, 3785.
[8] R. P. Bell and D. R. Marshall, *J. Chem. Soc.*, 1964, 2195.

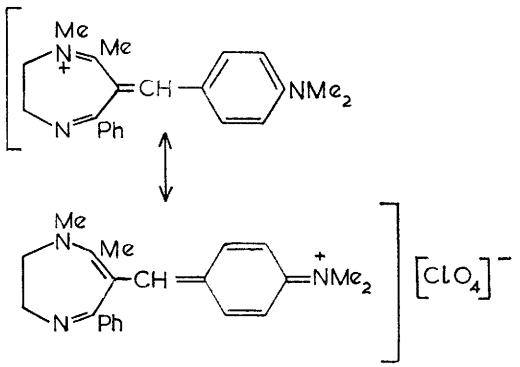
The cation of 2,3-dihydro-1,7-dimethyl-5-phenyl-1*H*-1,4-diazepine (V) was brominated normally to a 6-bromodihydrodiazepinium salt (VI) but treatment of the



(V) (VI) X^- (VII) Br^-

base with bromine in methanol gave a product (VII) with a different u.v. spectrum. On addition of perchloric acid to each, (VI) and (VII) formed perchlorates which were not identical (mixed m.p.), and whereas (VI) could be converted into the corresponding dihydrodiazepine base, (VII) gave only coloured decomposition products on treatment with alkali. Compound (VII) was stable in solution in trifluoroacetic acid, (VI) was not. The n.m.r. spectrum of (VII) confirmed that substitution had taken place at the 7-methyl group. The anomalous behaviour of (V) presumably results from the fact that, unlike *N*-unsubstituted dihydrodiazepines, it has a fixed structure, incapable of tautomeric rearrangement, and that in this structure the 7-methyl group is activated by conjugation with the azomethine group. When this bromomethyl compound was heated with piperidine, it was readily converted into a 7-*N*-piperidinylmethyl compound.

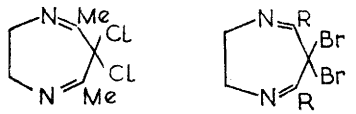
In order to investigate possible reactions of the cation of dihydrodiazepine (V), which might be indicative of a reactive methyl group, its perchlorate was heated with *p*-dimethylaminobenzaldehyde in acetic anhydride but, as with bromination of the cation, reaction took place at the 6-position to give the purple 6-*p*-dimethylaminobenzylidene compound (VIII), which owes its colour to its mesomeric character. It dissolves in trifluoroacetic acid to give a yellow solution, loss of colour being due to protonation, probably at the dimethylamino-group. Addition of methanol to this solution reprecipitates the original purple salt.



(VIII)

Iodination and Chlorination of Dihydrodiazepines.—Kinetic studies [8] showed that the dihydrodiazepinium cation could be iodinated, but no iodo-derivative had hitherto been isolated. The iodo-compounds are most readily prepared from the corresponding 6-bromo-compounds by heating the latter with sodium iodide in refluxing methanol, or by treatment of the unsubstituted dihydrodiazepinium salts with *N*-iodosuccinimide in refluxing chloroform.

Dihydrodiazepines are smoothly chlorinated by *N*-chlorosuccinimide in acetic acid to give 6-chlorodihydrodiazepines, but work-up of a reaction between chlorine and 2,3-dihydro-5,7-dimethyl-1*H*-1,4-diazepine gave only 3,3-dichloroacetylacetone. It thus appears that chlorine readily dichlorinates the diazepine and that



(IX) (X)

the dichloro-compound (IX), having two azomethine groups but no stable delocalised electron system as in the parent compound, is very easily hydrolysed.

Dibromination of Dihydrodiazepines.—Kinetic studies [8] suggested that dibromination of dihydrodiazepines in aqueous solution took place to give derivatives (X), but, owing to their ready hydrolysis, no dibromo-compounds were isolated, although a compound which was apparently 3,3-dibromoacetylacetone was obtained from the hydrolysis products of the dibrominated derivative of (I).[8]

6,6-Dibromo-2,3-dihydro-5,7-diphenyl-6*H*-1,4-diazepine (X; R = Ph) has now been obtained by bromination of its monobromo-analogue in dry benzene. Its i.r. spectrum did not show the characteristic diazepine N–H stretching absorption at 3200—3300 $cm.^{-1}$, its n.m.r. spectrum (in $CDCl_3$) showed only peaks at τ 2·3—2·6 (complex) and 5·72 (singlet) (10 : 4) and its elemental analysis was in accord with the assigned structure.

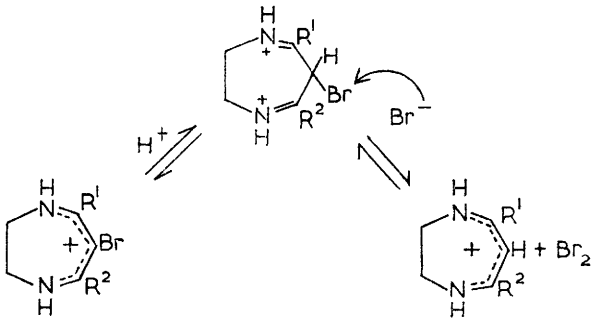
6-Bromo-6-chloro-2,3-dihydro-5,7-diphenyl-6*H*-1,4-diazepine was similarly obtained by bromination of the 6-chloro-compound and had similar i.r. and n.m.r. spectra to those of (IX).

Both dihalogeno-compounds were readily debrominated by dilute aqueous acid and their solutions in benzene gave immediate precipitates of the 6-bromodihydrodiazepinium salt on addition of dilute hydrobromic acid; bromine was also formed. This is another example of the great tendency for reversion to the mesomeric dihydrodiazepinium system. The debromination of 6-bromodihydrodiazepines is discussed further in the next sections.

Debromination of 6-Bromodihydrodiazepinium Salts in Acid.—From the n.m.r. spectra of solutions of 5,7-diphenyl- or 5-methyl-7-phenyl-6-bromo-2,3-dihydro-1*H*-1,4-diazepinium bromides in trifluoroacetic acid it was observed that the bromine atoms were rapidly replaced by hydrogen. If the perchlorates or trifluoroacetates were used no such exchange occurred. No debromin-

ation of the 6-bromo-5,7-dimethyl analogue took place under these conditions irrespective of the nature of the anion. However, debromination of the bromides of both the 5,7-dimethyl- and 5,7-diphenyl-6-bromodihydrodiazepinium salts occurred in concentrated sulphuric acid. Dilution of these solutions with water caused reformation of the 6-bromo-compounds, but if the dilution was carried out with dilute sodium thiosulphate solution, the debrominated compounds remained.

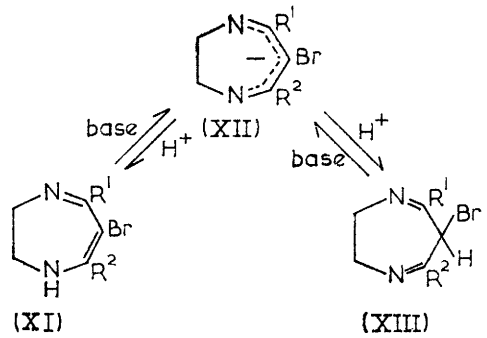
Debrominations of bromodihydrodiazepinium bromides in strong acid can be rationalised in terms of the equilibria:



In strong acid the dication is formed and this undergoes nucleophilic attack by bromide ion to give bromine and the debrominated monocation. On dilution the reverse reaction ensues, but addition of thiosulphate removes the bromine and prevents rebromination. If the anion is perchlorate or trifluoroacetate this will make no comparable attack on the bromine atom. The different acid strength required to debrominate, on the one hand the dimethyl, and on the other hand the methylphenyl and diphenyl compounds may reflect the difference in the basicity of the two monocations or, alternatively, the more ready loss of bromine in the more sterically crowded molecules. This debromination is comparable to the much smoother deiodination reaction.[8]

Reactions of 6-Bromodihydrodiazepines with Bases.—It has been demonstrated that the bromine atom in 6-bromo-2,3-dihydro-5,7-dimethyl-1*H*-1,4-diazepine is readily replaced by an ethoxy- or a methoxy-group by reaction with the appropriate alkoxide.[5] This ready nucleophilic substitution is surprising, since in the normal tautomeric form (XI) this position should be deactivated towards nucleophilic attack; indeed there is abundant evidence that the 6-position is a site where electrophilic substitution takes place readily.[2]

However, it is possible that in the presence of base prototropic rearrangement *via* the delocalised dihydrodiazepenide anion (XII) to the tautomer (XIII) will take place. Although the equilibrium concentration of (XIII) is likely to be small it would be strongly electrophilic at the 6-position owing to the combined effects of the bromine atom and the two adjacent electron-withdrawing azomethine groups, and it could well be the reactive species in nucleophilic substitution



of the bromine atom. A tautomer of this structure has never been observed with 2,3-dihydro-1*H*-1,4-diazepines but it represents the normal structure of 2,3-benzo-1*H*-1,4-diazepines[9] and equilibration between the two tautomeric forms has been recorded for benzodiazepines.[10]

Further investigation of the reactions between 6-bromodihydrodiazepines and nucleophiles showed that normal substitution in many instances did not occur, but that instead the bromine atom was replaced by a hydrogen atom. Some of these results are listed in Table. The 6-alkoxy- and 6-amino-dihydrodiazepines are not themselves intermediates in the formation of the debrominated compounds, which must be formed competitively, since 6-ethoxy- or 6-benzylamino-2,3-dihydro-5,7-diphenyldiazepines when heated with, respectively, ethoxide ion or benzylamine, give no 6-unsubstituted product.

The dihydrodiazepines themselves may act as the bases to bring about Br–H exchange, since when 6-bromo-5,7-diphenyldihydrodiazepine was heated in benzene, toluene, or ethanol, slow replacement of the bromine by hydrogen was observed. This may also explain the difference in reaction product which was noted in one case when different concentrations of diazepine were used (see the Table).

Dihydrodiazepine:	5,7-Me_2	5-Me, 7-Ph	5,7-Ph_2
Reagent			
MeO^-	N	N	N
EtO^-	N	N	H or H and N *
Pr^iO^-	H		
Bu^iO^-	H		
PhO^-	N		
Pyrrolidine	N	N	
Piperidine	N	N	N and H (4 : 1)
$PhCH_2NH_2$	†	‡	H

N = Normal nucleophilic substitution.
H = Replacement of bromine by hydrogen.
* = 0·1M-Dihydrodiazepine ⟶ H; 0·01M ⟶ N and H (50 : 50). † = No isolable product. ‡ = Low yield of 2-phenylimidazolinium bromide (formed by ring-contraction).

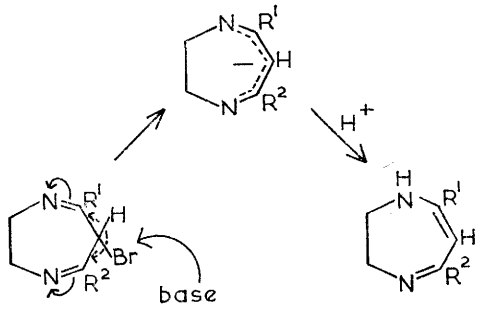
The mechanism of the 'abnormal' substitution of the bromine atom (*i.e.* by hydrogen) is obscure. The closest

[9] I. L. Finar, *J. Chem. Soc.*, 1958, 4094; J. A. Barltrop, C. G. Richards, D. M. Russell, and G. Ryback, *ibid.*, 1959, 1132.

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

analogies are the ready replacement of bromine by hydrogen in *N*-bromosuccinimide and some bromo-β-dicarbonyl compounds.

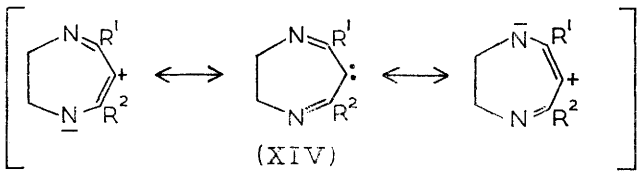
It is possible that the bisazomethine tautomer (XIII) is again involved. Nucleophilic attack at the bromine atom by base, which could either be added reagent or another diazepine molecule (as it must be when the diazepine is heated alone in a neutral solvent), leads to an anion which, in turn, extracts a proton either from solvent or from another diazepine molecule:



It may be noted that benzylamine, which would seem likely to be an effective agent in this type of reaction, gives notably higher yields of debrominated product.

The involvement of tautomer (XIII) is strongly suggested by the fact that under identical conditions *N*-methyldihydrodiazepines do not undergo this reaction. Under more vigorous conditions and with a longer reaction time, small amounts of debrominated product have been observed in one instance, and a small yield of 'normal' substitution product in another, but the markedly different reaction conditions required make it not unreasonable to assume that an alternative, less simple, reaction scheme is then involved.

An alternative general mechanism would involve the loss of a bromide ion from the anion (XII) to produce an electron-deficient species (XIV), a process having


(XIV)

some parallel in the formation of dichlorocarbene from the $(CCl_3)^-$ anion or of a nitrene in the Hofmann and related rearrangements. The difficulty in this case is that formation of the final product involves the addition of the equivalent of a proton and a hydride ion and a suitable source for the latter is difficult to envisage. In general, hydride-ion abstraction at any stage seems to be unlikely, for although isopropoxide ion in isopropyl alcohol or α-phenylethoxide ion in α-phenethanol were effective reagents in bringing about bromine-hydrogen exchange, neither acetone nor acetophenone could be detected among the products from the reactions.

Homolysis of the 6-(C–Br) bond to give a diazepine radical also seems unlikely since (*a*) added base accelerates the reaction and (*b*) when debromination is carried out by heating the bromodihydrodiazepine in toluene no trace of dibenzyl could be detected by g.l.c. of the reaction mixture.

The results obtained suggest, in a general way, that steric factors affect the course of the reaction. If the bisazomethine tautomer is the reactive species in both normal and abnormal substitution in the manner suggested, it is not unreasonable that the abnormal reaction, which has less steric demands, might be favoured in the cases of more bulky diazepines or nucleophiles.

The reactions of methoxide ion with 6-bromo-2,3-dihydro-5-methyl-7-phenyl-1*H*-1,4-diazepine and 6-bromo-2,3-dihydro-5,7-diphenyl-1*H*-1,4-diazepine were studied kinetically and shown to be normal bimolecular substitution reactions, both proceeding at similar rates. The rates of reaction were followed by recording the absorbance of the solutions at 265 mμ since there is a marked difference in the absorbance of the bromo- and methoxy-dihydrodiazepines at this wavelength.

EXPERIMENTAL

N.m.r. spectra were recorded in trifluoroacetic acid unless an alternative solvent is specified. U.v. spectra were recorded in methanol or ethanol unless otherwise indicated.

Bromination of 2,3-*Dihydro*-1H-1,4-*diazepines.—Method* (a). An equimolar quantity of bromine in methanol or chloroform was added gradually to a solution of the dihydrodiazepine in the same solvent. Addition of ether then precipitated the bromodihydrodiazepinium bromide.

Method (b): An equimolar quantity of bromine in methanol was added gradually to a solution of the dihydrodiazepinium perchlorate in methanol. The bromodihydrodiazepinium salts were precipitated by addition of ether and had a mixture of bromide and perchlorate anions. Addition of concentrated aqueous sodium hydroxide converted the salts into the bromo-base, which was extracted with ether or benzene. Removal of dried solvent gave the base, which was converted into the perchlorate by addition of an equimolar amount of perchloric acid (60%). By these means the following bromodihydrodiazepines were prepared, in yields ranging from 60 to 93%: 6-*bromo*-2,3-*dihydro*-1,5,7-*trimethyl*-1H-1,4-*diazepinium perchlorate*, m.p. 133—134° (from methanol), τ 2·0 (broad), 6·1, 6·5, 7·35, 7·45 (1 : 4 : 3 : 3 : 3) (Found: C, 30·5; H, 4·6. $C_8H_{14}BrClN_2O_4$ requires C, 30·3; H, 4·4%); 6-*bromo*-2,3-*dihydro*-2,5,7-*trimethyl*-1H-1,4-*diazepinium bromide*, m.p. 180—181° (from ethanol) τ 1·6 (v. flat), 6·1, 6·4.(d), 7·3, 8·6.(d) (2 : 1 : 2 : 6 : 3) (Found: C, 31·9; H, 4·3; Br, 54·2. $C_8H_{14}Br_2N_2$ requires C, 32·2; H, 4·7; Br, 53·7%); 6-*bromo*-2,3-*dihydro*-2,2,5,7-*tetramethyl*-1H-1,4-*diazepinium bromide*, m.p. 117—119° (from ethanol) (Found: C, 34·7; H, 5·4; Br, 51·5; N, 8·9. $C_9H_{16}Br_2N_2$ requires C, 34·6; H, 5·1; Br, 51·3; N, 9·0%); 6-*bromo*-2,3-*dihydro*-1,7-*dimethyl*-5-*phenyl*-1H-1,4-*diazepinium perchlorate*, m.p. 145—146° (from methanol), τ 2·1 (broad), 2·6, 5·4 (m), 6·0 (m), 6·4, 7·2 (1 : 5 : 2 : 2 : 3 : 3) (Found: C, 41·4; H, 4·4; N, 7·4. $C_{13}H_{16}BrClN_2O_4$ requires C, 41·1; H, 4·3; N, 7·4%); 6-*bromo*-2,3-*dihydro*-1-*methyl*-5,7-*diphenyl*-1H-1,4-*diazepin*-

ium perchlorate, m.p. 165—168° (from water) τ 2·0 (broad), 2·5, 5·8, 6·7 (1 : 10 : 4 : 3) (Found: C, 49·2; H, 4·2; Br, 18·4; N, 6·5. $C_{18}H_{18}BrClN_2O_4$ requires C, 49·0; H, 4·1; Br, 17·9; N, 6·4%); dihydrodiazepine base, m.p. 89—91°; 6-*bromo*-2,3-*dihydro*-5-*methyl*-7-*phenyl*-1H-1,4-*diazepinium bromide*, m.p. 175—178°, τ 1·4 (broad), 2·4, 6·05 (m), 7·25 (2 : 5 : 4 : 3) (Found: Br, 46·2. $C_{12}H_{14}Br_2N_2$ requires Br, 47·4%); 6-*bromo*-2,3-*dihydro*-5,7-*diphenyl*-1H-1,4-*diazepinium bromide*, m.p. 178—180° (from ethanol), τ 1·7 (broad) 2·45, 5·85 (m), (2 : 10 : 4) (Found: C, 49·5; H, 4·0; Br, 39·4. $C_7H_{16}Br_2N_2$ requires C, 50·0; H, 4·0; Br, 39·2%), dihydrodiazepine base, m.p. 158—161° (from ethanol), perchlorate, m.p. 177° (from ethanol); 6-*bromo*-2,3-*dihydro*-5-p-*nitrophenyl*-7-*phenyl*-1H-1,4-*diazepinium bromide*, m.p. 192—197° (from ethanol), perchlorate, m.p. 180—182° (from ethanol), τ 1·1, 1·5—2·2, 2·4, 5·75 (2 : 4 : 5 : 4).

Bromination of 2,3-*Dihydro*-5,7-*dimethyl*-1,4-*diphenyl*-1H-1,4-*diazepinium Perchlorate*.—When carried out by the method described in the previous section, bromination produced a mixture of products, crude m.p. 120—170°, $\lambda_{max.}$ 349 mμ. When bromine (1·5 g., 7 equiv.) in methanol was added gradually to the perchlorate (0·5 g.) in methanol, a precipitate formed. Recrystallisation from methanol gave a product (0·54 g.), m.p. 137—144°, $\lambda_{max.}$ 376 mμ (Found: C, 35·8; H, 3·2; N, 4·5. $C_{19}H_{18}Br_4N_2$ requires C, 38·4; H, 3·6; N, 4·7. $C_{19}H_{17}Br_5N_2$ requires C, 33·9; H, 3·1; N, 4·2%). This product was warmed with hydrobromic acid (3 ml.) and methanol (15 ml.). The precipitate which formed was removed and stirred for 10 min. with aqueous sodium hydroxide (1·5 g./4 ml.). T.l.c. of the product indicated at least five components. It was concluded that the major product was bis-(2,4-dibromoanilino)ethane from its m.p. 139—140°, (lit.,[11] 140°) and from the resemblance of its n.m.r. spectrum, τ 1·97—2·44, 5·7 (6 : 4), to that of 2,4-dibromoaniline but not to that of 2,6-dibromoaniline (Found: C, 32·9; H, 2·4; N, 5·3; Br, 59·7. Calc. for $C_{14}H_{12}Br_4N_2$: C, 31·9; H, 2·3; N, 5·3; Br, 60·5%).

7-*Bromomethyl*-2,3-*dihydro*-1-*methyl*-5-*phenyl*-1H-1,4-*diazepinium Bromide* (VII).—A molar equivalent of bromine in methanol was added to 2,3-dihydro-1,7-dimethyl-5-phenyl-1*H*-1,4-diazepine (V) (1·6 g.) in methanol (10 ml.). The solvent was removed under reduced pressure and the residue was triturated with acetone. Crystals of the *bromide* (VII) (1·28 g., 44%) were obtained, m.p. 215—217° (from methanol), τ 1·75 (broad), 2·38, 4·3, 5·86, 5·93, 6·04, 6·93 (1 : 5 : 1 : 2 : 2 : 2 : 3) (Found: C, 43·3; H, 4·9; N, 7·9. $C_{13}H_{16}Br_2N_2$ requires C, 43·3; H, 4·5; N, 7·8%). Methanolic perchloric acid gave the perchlorate, m.p. 157—159°. Attempts to form and isolate the base led only to purple–brown decomposition products. When heated with piperidine, (VII) gave the corresponding 7-*N*-piperidinylmethyl dihydrodiazepinium bromide, m.p. 199—202°, τ 1·5 (broad) 2·37, 4·18, 5·4—6·2(m), 6·32, 8·0(m) (1 : 5 : 1 : 10 : 3 : 6).

6-p-*Dimethylaminobenzylidene*-2,3-*dihydro*-1,7-*dimethyl*-5-*phenyl*-6H-1,4-*diazepinium Perchlorate* (VIII).—2,3-Dihydro-1,7-dimethyl-5-phenyl-1*H*-1,4-diazepinium perchlorate (2 g.) and *p*-dimethylaminobenzaldehyde (1 g.) were heated in acetic anhydride (20 ml.) at reflux temperature for 1½ hr. Ether (500 ml.) was added to the cooled reaction mixture, and the precipitated salts were recrystallised from methanol, to give purple crystals of the *perchlorate* (VIII) (0·75 g., 26%), m.p. 227—228°, τ 1·8—2·9 (m), 5·2 (m), 5·5 (m), 6·02, 6·44, 8·00 (10 : 2 : 2 : 3 : 6 : 3) (Found: C, 60·8 ; H; 6·2. $C_{22}H_{26}ClN_3O_4$ requires C, 61·2; H, 6·3%).

2,3-*Dihydro*-6-*iodo*-5,7-*dimethyl*-1H-1,4-*diazepinium Salts*.—(*a*) The corresponding 6-bromo-compound (3·0 g.) and sodium iodide (6·0 g.) were heated to reflux in methanol (30 ml.). When cooled the solution gave the iododihydrodiazepinium bromide as yellow crystals (2·13 g., 60%), m.p. 175—177° from methanol–ethyl acetate. Addition of perchloric acid in methanol gave the pale yellow *perchlorate*, m.p. 168—170° (Found: I, 37·1; N, 8·1. $C_7H_{12}ClIN_2O_4$ requires I, 37·0; N, 8·0%). (*b*) 2,3-Dihydro-5,7-dimethyl-1*H*-1,4-diazepinium perchlorate (1·0 g.) and *N*-iodosuccinimide (1·1 g.) were heated in refluxing chloroform (20 ml.) for 1½ hr. The mixture was cooled and the precipitated solid was filtered off, washed with chloroform, dried and recrystallised twice from water to give the iododihydrodiazepinium perchlorate, m.p. 171° (1·05 g., 67%) (Found: C, 23·8; H, 3·4; N, 7·9. $C_7H_{12}ClIN_2O_4$ requires C, 24·0; H, 3·5; N, 8·0%).

6-*Chloro*-2,3-*dihydro*-5,7-*dimethyl*-1,4-*diphenyl*-1H-1,4-*diazepinium Perchlorate*.—The unsubstituted diazepinium perchlorate (2·5 g.) and *N*-chlorosuccinimide (0·64 g.) were heated in refluxing acetic acid (40 ml.) for 2 hr. Solvent was then removed under reduced pressure and the product was crystallised from ethanol to give yellow–green needles of the *chlorodihydrodiazepinium perchlorate* (1·4 g., 51%), m.p. 150—151°, τ 2·5, 5·6, 7·35 (10 : 4 : 6) (Found: Cl, 16·5; N, 6·6. $C_{19}H_{20}Cl_2N_2O_4$ requires Cl, 17·3; N, 6·8%).

6-*Chloro*-2,3-*dihydro*-5,7-*diphenyl*-1H-1,4-*diazepine*.—2,3-Dihydro-5,7-diphenyl-1*H*-1,4-diazepine (1·5 g.) and *N*-chlorosuccinimide (0·81 g.) were heated in refluxing acetic acid (45 ml.) for 2 hr. Most of the solvent was then removed under reduced pressure. Addition of water (25 ml.) and concentrated hydrochloric acid (3 ml.) precipitated the hydrochloride of the 6-chloro-dihydrodiazepine (1·7 g., 87·5%), m.p. 263°, τ 1·6, 2·45, 5·93 (2 : 10 : 4). Aqueous sodium hydroxide (20%, 20 ml.) was added to a hot aqueous solution of the hydrochloride (1·7 g./20 ml.) and the mixture was extracted with benzene (3 × 50 ml.). Some solvent was removed to leave a solution (5 ml.) which when cooled, gave crystals of 6-*chloro*-2,3-*dihydro*-5,7-*diphenyl*-1H-1,4-*diazepine* (1·32 g., 88%), m.p. 192—193° (Found: C, 72·4; H, 5·5. $C_{17}H_{15}ClN_2$ requires C, 72·2; H, 5·3%).

6-*Halogeno*-2,3-*dihydro*-5-*methyl*-7-*phenyl*-1H-1,4-*diazepinium Perchlorates*.—(*a*) 2,3-Dihydro-5-methyl-7-phenyl-1*H*-1,4-diazepinium perchlorate monohydrate (2·9 g.) and *N*-chlorosuccinimide (1·3 g.) were heated in boiling chloroform (25 ml.) for 1½ hr. Solvent was evaporated off and the residue was recrystallised twice from water to give 6-*chloro*-2,3-*dihydro*-5-*methyl*-7-*phenyl*-1H-1,4-*diazepinium perchlorate*, m.p. 180—184° (2·6 g., 86%), τ *ca.* 1·2—2·0, 2·2, 5·9, 7·3 (2 : 5 : 4 : 3) (Found: C, 44·8; H, 4·4; N, 8·8. $C_{12}H_{14}N_2Cl_2O_4$ requires C, 44·9; H, 4·4; N, 8·7%).

(*b*) When *N*-bromosuccinimide replaced *N*-chlorosuccinimide in the above reaction, 6-*bromo*-2,3-*dihydro*-5-*methyl*-7-*phenyl*-1H-1,4-*diazepinium perchlorate* was obtained, m.p. 174—176° (2·15 g., 63%), τ (Me_2SO) 2·2, 6·15, 7·4 (5 : 4 : 3), N*H* signals too broad to detect with certainty (Found: C, 39·0; H, 3·8; N, 7·7. $C_{12}H_{14}N_2BrClO_4$ requires C, 39·4; H, 3·9; N, 7·7%).

(*c*) 2,3-Dihydro-5-methyl-7-phenyl-1*H*-1,4-diazepinium perchlorate (0·64 g.) and *N*-iodosuccinimide (0·50 g.) were heated in boiling chloroform for 30 min. The mixture was cooled and filtered and the resultant yellow solid was

[11] A. E. Schouten, *Rec. Trav. chim.*, 1937, **56**, 863.

recrystallised from water to give the 6-*iododihydrodiazepinium perchlorate*, m.p. 221—223° (decomp.) (variable, dependent on rate of heating; present value obtained by pre-heating block to *ca.* 200° and then heating at a moderate rate) (0·64 g., 69%), τ (Me_2SO) 2·2, 6·15, 7·25 (5 : 4 : 3), N*H* signals too broad to detect with certainty (Found: C, 35·0; H, 3·5; N, 6·8. $C_{12}H_{14}N_2ClIO_4$ requires C, 34·9; H, 3·4; N, 6·8%).

Chlorination with Chlorine.—Chlorine gas was passed into a dry ethereal solution of 2,3-dihydro-5,7-dimethyl-1*H*-1,4-diazepine. The colourless solid product became oily on attempted filtration and yielded 3,3-dichloroacetylacetone. The same product, together with 3-chloroacetylacetone was obtained when chlorine water reacted with the diazepine.

6,6-*Dibromo*-2,3-*dihydro*-5,7-*diphenyl*-6H-1,4-*diazepine.*—Bromine (0·7 g.) was added gradually to a stirred solution of 6-bromo-2,3-dihydro-5,7-diphenyl-1*H*-1,4-diazepine (1·31 g.) in benzene (150 ml.). 6-Bromo-2,3-dihydro-5,7-diphenyl-1*H*-1,4-diazepinium bromide (0·81 g., 49·7%) was precipitated and was filtered off. Benzene was distilled from the filtrate at reduced pressure to leave a residue which, after recrystallisation from ethanol, gave the *dibromodihydrodiazepine* (0·66 g., 41%), m.p. 119—120°, τ ($CDCl_3$) 2·3—2·6 (m), 5·72 (10 : 4), i.r. peaks (hexachlorobutadiene mull) at 1640, 1480, 1440, 1350, 1320, 1310, 1280, 1240, 1220, 1080, 1035, 920, 900, 897, 760, 735, and 690 $cm.^{-1}$ (Found: C, 49·8; H, 3·3. $C_{17}H_{14}Br_2N_2$ requires C, 50·3; H, 3·5%).

6-*Bromo*-6-*chloro*-2,3-*dihydro*-5,7-*diphenyl*-6H-1,4-*diazepine*. A solution of 6-chloro-2,3-dihydro-5,7-diphenyl-1*H*-1,4-diazepine (0·28 g.) in dry benzene (20 ml.) was treated with slightly more than a molar equivalent of bromine (0·2 g.). The precipitated chlorodihydrodiazepinium bromide was filtered off; removal of solvent from the filtrate and recrystallisation of the residue from methanol gave the pale yellow bromochloro-compound (0·09 g. 25%), m.p. 97—99°. Its identity followed from a comparison of its i.r. and n.m.r. spectra with those of the corresponding 6,6-dibromo-compound τ ($CDCl_3$), 2·3—2·6 (m), 5·70 (10 : 4), i.r. peaks at 1640, 1480, 1440, 1420, 1350, 1320, 1300, 1280, 1240, 1220, 1080, 1065, 1035, 920, 895, 755, and 695 $cm.^{-1}$.

Debromination of 6,6-*Dibromo*-2,3-*dihydro*-5,7-*diphenyl*-6H-1,4-*diazepine.*—Addition of dilute aqueous hydrobromic acid to a solution of the dibromo-compound in benzene caused immediate precipitation of the monobromo-compound; the benzene layer contained bromine.

Debromination of 6-*Bromo*-2,3-*dihydro*-1H-1,4-*diazepinium Cations in Acid Solution.*—(*a*) Solutions of 5,7-dimethyl-, 5-methyl-7-phenyl-, and 5,7-diphenyl-6-bromo-2,3-dihydro-1*H*-1,4-diazepinium bromides in trifluoroacetic were prepared and set aside for 10 min. before their n.m.r. spectra were determined. The spectra indicated that 0%, 30%, and 65%, respectively, of the bromo-compounds had been converted into their debrominated analogues.

(*b*) The n.m.r. spectra of solutions of 6-bromo-2,3-dihydro-5,7-diphenyl-1*H*-1,4-diazepine and its perchlorate in trifluoroacetic acid were observed at intervals over a period of 1 week. No change occurred, the spectra being solely those of the 6-bromo-cations. The addition of a small crystal of potassium chloride to each solution brought about *ca.* 20% conversion into the debrominated compound after 1 hr. at room temperature and no further change occurred during 20 days. Addition of solid sodium bromide then brought about further conversion into the debrominated compound, reaction being complete within 1 hr.

(*c*) Solutions of 5,7-dimethyl- and 5,7-diphenyl-6-bromo-2,3-dihydro-1*H*-1,4-diazepinium bromides (3 mg. and 4 mg. respectively) were made in concentrated sulphuric acid (1 ml.); their u.v. spectra indicated the presence of the debrominated dication [no absorption > 200 mμ; and $\lambda_{max.}$ 290 mμ (ε 23,500)]. After 24 hr. aliquots (0·5 ml.) of the solutions were diluted with water (100 ml.) and the u.v. spectra were recorded immediately. The spectra were characteristic of the 6-bromo-monocations [$\lambda_{max.}$ 257 and 347·5 mμ (ε 1000 and 12,210); $\lambda_{max.}$ 240, 263, and 373 mμ (ε 7000, 7000, and 15,460)]. The remaining solutions (0·5 ml.) were diluted with aqueous sodium thiosulphate (0·01M; 100 ml.) and the u.v. spectra were recorded immediately. The spectra were characteristic of the debrominated monocations [$\lambda_{max.}$ 260 and 323 mμ (ε 1500 and 16,570); $\lambda_{max.}$ 268 and 358 mμ (ε 14,070 and 22,955)].

2,3-*Dihydro*-6-*methoxy*-5,7-*diphenyl*-1H-1,4-*diazepinium Perchlorate.*—The corresponding 6-bromodiazepine (0·327 g.) was heated with potassium methoxide in methanol (M; 10 ml.) at reflux temperature for 30 min. Methanol was removed, water was added (2 ml.) and the mixture was extracted with benzene (3 × 5 ml.). After drying and removal of benzene, the 6-methoxydihydrodiazepine was obtained, m.p. 177—178·5°. Addition of perchloric acid (60%; 0·15 ml.) in water (0·5 ml.) gave the yellow *perchlorate* (0·24 g., 63%), m.p. 238—240° (from methanol), $\lambda_{max.}$ 265 and 377 mμ (ε 9860 and 17,080), τ 2·0 (broad), 2·4, 5·95, 6·85 (2 : 10 : 4 : 3) (Found: C, 57·1; H, 4·8; N, 7·4. $C_{18}H_{19}ClN_2O_5$ requires C, 57·1; H, 5·1; N, 7·4%).

2,3-*Dihydro*-6-*methoxy*-5-*methyl*-7-*phenyl*-1H-1,4-*diazepinium Perchlorate.*—Prepared as the previous compound, but from the corresponding 6-bromodihydrodiazepinium bromide (3·46 g.), the *perchlorate* (2·6 g., 82%), m.p. 166—168° (from methanol), had $\lambda_{max.}$ 265 and 367 mμ (ε 6680 and 16,030), τ 2·0 (broad), 2·4, 6·1, 6·6, 7·45 (2 : 5 : 4 : 3 : 3) (Found: C, 49·4; H, 5·8. $C_{13}H_{17}ClN_2O_5$ requires C, 49·4; H, 5·4%).

2,3-*Dihydro*-6-*ethoxy*-5-*methyl*-7-*phenyl*-1H-1,4-*diazepinium Perchlorate.*—Prepared as the methoxide from the bromodihydrodiazepinium bromide (0·346 g.) and potassium ethoxide in ethanol (M; 10 ml.), the *perchlorate* (0·247 g., 75%) had m.p. 166—168° (from ethanol), $\lambda_{max.}$ 260 and 367 mμ (ε 7240 and 14,530), τ 2·0—2·6, 2·35, 6·1, 6·35 (q), 7·45, 9·0 (t) (2 : 5 : 4 : 2 : 3 : 3) (Found: N, 8·3. $C_{14}H_{19}ClN_2O_5$ requires N, 8·5%).

2,3-*Dihydro*-5,7-*dimethyl*-6-*phenoxy*-1H-1,4-*diazepinium Chloride.*—The corresponding 6-bromo-compound (5 g.) and sodium phenoxide (1·1 g.) were heated in refluxing anhydrous ethanol for 2 hr. Sodium bromide was filtered off, solvent was removed by distillation, and aqueous sodium hydroxide (10%, 50 ml.) was added to the residue; the mixture was extracted with ether. On passing hydrogen chloride through the ether extract, the *phenoxydihydrodiazepinium chloride* was precipitated, m.p. >250° (from ethanol–ethyl acetate), τ −0·6, 2·9, 6·3, 7·75 (2 : 5 : 4 : 6). (Found: C, 62·5; H, 7·0; N, 10·9. $C_{13}H_{17}ClN_2O$ requires C, 61·8; H, 6·7; N, 11·1%).

2,3-*Dihydro*-5,7-*dimethyl*-6-N-*piperidinyl*-1H-1,4-*diazepinium Perchlorate.*—6-Bromo-2,3-dihydro-5,7-dimethyl-1*H*-1,4-diazepine (10·5 g.) and piperidine (50 ml.) were heated at 60° for 1 hr. Piperidine was removed under reduced pressure and warm water (10 ml.) was added to the residue, followed by perchloric acid (60%; 10 ml.).

The precipitate was recrystallised from water to give the yellow *perchlorate* (13·6 g., 95%), m.p. 268—270°, $\lambda_{max.}$ (H_2O) 340 mμ (ε 7250), τ 1·2 (broad), 6·05 (m), 7·2, 7·8 (m) (2 : 8 : 6 : 6) (Found: C, 47·1; H, 7·4; N, 13·4. $C_{12}H_{22}ClN_3O_4$ requires C, 46·8; H, 7·2; N, 13·6%). Addition of perchloric acid (60%) to the monoperchlorate gave a colourless diperchlorate, m.p. 200—205° (decomp.), which reverted to the monoperchlorate in aqueous solution.

2,3-*Dihydro*-5-*methyl*-7-*phenyl*-6-N-*piperdinyl*-1H-1,4-*diazepinium Perchlorate*.—Prepared as the previous compound from the corresponding bromodihydrodiazepine (1 g.) and piperidine (5 g.), the orange–yellow *perchlorate* (1·2 g., 86%), had m.p. 211—213° (from methanol), τ 0·8 (broad), 1·2 (broad), 2·15, 5·9, 6·1 (m), 7·1, 7·7—9·2 (m) (1 : 1 : 5 : 4 : 4 : 3 : 6) (Found: C, 55·6; H, 6·4; N, 11·4. $C_{17}H_{24}ClN_3O_4$ requires C, 55·2; H, 6·5; N, 11·4%).

2,3-*Dihydro*-5,7-*dimethyl*-6-N-*pyrrolidinyl*-1H-1,4-*diazepinium Perchlorate*.—6-Bromo-2,3-dihydro-5,7-dimethyl-1*H*-1,4-diazepine (1·42 g.) was heated with pyrrolidine (20 ml.) at 60° for 1 hr. Excess of pyrrolidine was distilled off at reduced pressure and water (20 ml.) added to the residue, followed by perchloric acid (60%; 3 ml.). Concentrated aqueous sodium hydroxide was then added dropwise until a pH of 10 was obtained whereupon 2,3-*dihydro*-5,7-*dimethyl*-6-N-*pyrrolidinyl*-1H-1,4-*diazepinium perchlorate* was precipitated (0·98 g., 48%), m.p. 159—160° (from water), τ 1·2 (broad), 6·0 (m), 6·05, 7·25, 7·5 (m) (2 : 4 : 4 : 6 : 4) (Found: C, 45·6; H, 6·8. $C_{11}H_{20}ClN_3O_4$ requires C, 45·0; H, 6·9%).

2,3-*Dihydro*-5-*methyl*-7-*phenyl*-6-N-*pyrrolidinyl*-1H-1,4-*diazepinium Perchlorate*.—The corresponding 6-bromo-compound (1 g.) was heated with pyrrolidine (10 ml.) at 60° for 1 hr. Excess of pyrrolidine was distilled off under reduced pressure and perchloric acid (10%, 6 ml.) was added to the residue. Water was then added dropwise until the *pyrrolidinyldihydrodiazepinium perchlorate* separated as orange–yellow crystals (0·73 g., 75%), m.p. 210—212°, τ 0·95 (broad), 1·3 (broad), 2·2, 5·9 (m), 7·15, 7·8 (1 : 1 : 5 : 8 : 3 : 4) (Found: C, 53·4; H, 6·3. $C_{16}H_{22}ClN_3O_4$ requires C, 54·0; H, 6·2%).

Reaction of 6-*Bromo*-2,3-*dihydro*-5,7-*dimethyl*-1H-1,4-*diazepine with Potassium Isobutoxide and Isopropoxide*.—The bromo-compound (1·42 g.) was heated under reflux for 20 min. with potassium isobutoxide (2·5 g.) in isobutyl alcohol (50 ml.). Isobutyl alcohol was removed under reduced pressure, and water (10 ml.) was added to the residue, which was extracted with ether (5 × 20 ml.). Removal of ether from the extract, followed by addition of perchloric acid (30%, 2 ml.) gave the debrominated perchlorate (0·29 g., 26%), m.p. 138—140°, authenticated by mixed m.p. and i.r. spectrum. A similar experiment using potassium isopropoxide in isopropyl alcohol gave 39% of the debrominated compound but no acetone could be detected and fractional distillation of the reaction mixture into a solution of 2,4-dinitrophenylhydrazine produced no precipitate.

Reaction of 6-*Bromo*-2,3-*dihydro*-5,7-*diphenyl*-1H-1,4-*diazepine with Sodium Ethoxide*.—The bromo-compound (0·327 g.; 0·1M) was heated in refluxing sodium ethoxide in ethanol (M; 10 ml.) for 30 min. Ethanol was distilled off under reduced pressure and water (2 ml.) was added. Extraction with benzene (4 × 5 ml.) and removal of the solvent left the debrominated dihydrodiazepine, m.p. 155—158° (0·105 g., 42%). It was identified by a mixed m.p., its i.r. spectrum, and conversion into its perchlorate, m.p. 154—156°. The same procedure, except for an initial heating time of 24 hr., gave a 46% yield of debrominated product. When the bromodihydrodiazepine concentration was 0·01 M (0·327 g./100 ml. M ethoxide) a mixture of 6-unsubstituted and 6-ethoxy-products was obtained. If the mixture was heated for 30 min. the yields of products were 6-unsubstituted, 35%; 6-EtO, 34% (calc. from n.m.r. spectrum of mixture); if instead it was kept at room temperature for 1 week, the yields of products were 6-unsubstituted, 29%; 6-EtO, 39%.

Reaction of 6-*Ethoxy*-2,3-*dihydro*-5,7-*diphenyl*-1H-1,4-*diazepine with Sodium Ethoxide*.—When the mixture of products from the last experiment was heated with M-sodium ethoxide in ethanol for 1 hr. and worked up as above, the ratio of 6-unsubstituted and 6-EtO products was unchanged; recovery >80%.

Reaction of 6-*Bromo*-2,3-*dihydro*-5,7-*diphenyl*-1H-1,4-*diazepine with Piperidine*.—The bromo-compound (0·327 g.) was heated in piperidine at 60° for 1 hr. After removal of excess of piperidine, addition of perchloric acid (60%; 1 ml.) followed by water (10 ml.) precipitated an orange solid (0·42 g.) the n.m.r. spectrum of which showed it to be a 4 : 1 mixture of 6-*N*-piperidinyl- and 6-unsubstituted dihydrodiazepinium perchlorates.

Reaction of 6-*Bromo*-2,3-*dihydro*-5,7-*diphenyl*-1H-1,4-*diazepine with Sodium* α-*Phenylethoxide*.—This reaction was carried out at 100° under nitrogen for 30 min. and produced *ca.* 40% of debrominated product. At intervals of 5 min. samples were withdrawn and examined for the presence of acetophenone by t.l.c. on silica, eluting with ether–light petroleum (b.p. 40—60°) (1 : 4) and developing by spraying with a solution of 2,4-dinitrophenyl-hydrazine in methanolic sulphuric acid. No acetophenone was found, although it was easily detected when applied to the plate in concentrations comparable to those expected were it a reaction product.

Reaction of 6-*Bromo*-2,3-*dihydro*-1H-1,4-*diazepines with Benzylamine*.—The bromodihydrodiazepines were heated with benzylamine (1 ml.) at 100° for 30 min. and ether was then added to the cooled reaction mixture. The 5,7-dimethyl derivative (0·2 g.) gave only dark resinous material; the 5-methyl-7-phenyl derivative (0·53 g.) gave resinous material which on trituration with ethanol–ether–acetone deposited crystals of 2-phenyl-imidazolinium bromide (0·042 g., 10%), m.p. and mixed m.p. with an authentic specimen [12] 201—202°, τ 1·6 (broad) 2·1 (m), 5·64 (2 : 5 : 4), correct i.r. spectrum. The 5,7-diphenyl derivative (0·654 g.) gave crystals of the corresponding 6-unsubstituted dihydrodiazepinium bromide (0·579 g., 88%), m.p. and mixed m.p. 270°. When the ethereal filtrate was added to 2,4-dinitrophenylhydrazine in aqueous ethanolic sulphuric acid, benzaldehyde 2,4-dinitrophenylhydrazone was precipitated (0·42 g., 75%), m.p. and mixed m.p. 235—236°.

Treatment of 6-*Benzylamino*-2,3-*dihydro*-5,7-*diphenyl*-1H-1,4-*diazepinium Perchlorate with Benzylamine*.—The perchlorate [4] (0·1 g.) was heated in benzylamine (3 ml.) at 100° for 30 min. After cooling and dilution with ether, the benzylaminodihydrodiazepinium perchlorate was recovered in essentially quantitative yield.

Reactions of 6-*Bromo*-2,3-*dihydro*-5,7-*diphenyl*-1H-1,4-*diazepine when heated in Neutral Solvents*.—The diazepine (0·327 g.) was heated at reflux in different solvents (10 ml.). After 24 hr. in ethanol, the solvent was removed and the

[12] R. Forsyth, V. K. Nimkar, and F. L. Pyman, *J. Chem. Soc.*, 1926, 800.

residue was extracted with hot benzene (3 × 10 ml.) to remove starting material. This left the 6-unsubstituted dihydrodiazepinium bromide (0·081 g., 24%), m.p. 265—268°. After 24 hr. in benzene, a precipitate (0·096 g., 29%) of the same product was obtained. After being heated for 2 hr. in toluene the yield of debrominated product was (0·126 g., 38%). G.l.c. of the toluene filtrate showed the absence of dibenzyl.

Reactions of 6-*Bromo*-1-*methyl*-2,3-*dihydro*-1H-1,4-*diazepines with Bases*.—The 5,7-diphenyl-, 7-methyl-5-phenyl- and 5,7-dimethyl-derivatives were heated with piperidine, cooled, and excess of amine was removed; aqueous perchloric acid was added to the residue. After 1 hr. at 60°, the only product from the 7-methyl-5-phenyl compound was starting material (81%); the diphenyl compound (0·441 g.) gave only starting material after 4 hr. at 60°, but after 24 hr. at reflux temperature some debrominated product had been formed (0·08 g., 18%). After 1 hr. at 60° the dimethyl compound (10 g.) produced some 2,3-*dihydro*-1,5,7-*trimethyl*-6-N-*piperidinyl*-1H-1,4-*diazepinium perchlorate* (0·12 g., 7%), m.p. 122—123° (from ethanol), τ 2·1 (broad), 5·9 (m), 6·4, 7·27, 7·30, 7·8 (1 : 8 : 3 : 3 : 3 : 6) (Found: C, 48·7; H, 7·5; N, 13·1. $C_{13}H_{24}ClN_3O_4$ requires C, 48·5; H, 7·5; N, 13·1%).

The above diazepines were also heated to reflux in M-methanolic sodium methoxide. After removal of solvent, perchloric acid was added to the residue, and any precipitate was filtered off. The 5,7-diphenyl compound gave only starting material after 4 hr. (86%) whilst the 7-methyl-5-phenyl compound gave starting material (58%) plus tars. The 5,7-dimethyl compound also gave only starting material (57%) but the ether extract of the residue in another experiment gave material which, from its n.m.r. spectrum, contained small amounts of the corresponding 6-unsubstituted and 6-methoxy-compounds.

Kinetic Studies of the Reactions between Bromodihydrodiazepines and Methoxide Ions.—The rates of reaction were observed by means of u.v. spectroscopy, noting the absorbance at 265 mμ, at which wavelength the initial bromo-compounds and the resultant methoxy-compounds have markedly different absorbances. By recording the change in absorbance with time the pseudo-first order rate constant k_1 was obtained, and a plot of k_1 against methoxide concentration gave the bimolecular rate constant k_2. Hence values for k_2 at 25° for the reactions between methoxide and 6-bromo-2,3-dihydro-5-methyl-7-phenyl-1*H*-1,4-diazepine and 6-bromo-2,3-dihydro-5,7-diphenyl-1H-1,4-diazepine were, respectively, $8·5 \times 10^{-5}$ and $8·0 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$.

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