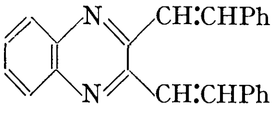
358. *The Phenazine Series. Part V. Reactions of* 1 : 2 : 3 : 4-*Tetrahydrophenazine and Related Compounds.*

By Henry McIlwain.

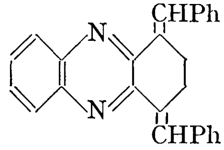
1- and 1 : 4-Substituted phenazine derivatives can be prepared from 1 : 2 : 3 : 4-tetrahydrophenazine by condensation with aromatic aldehydes. The methiodides of the tetrahydrophenazine and of *s*-octahydrophenazine do not undergo the varied ionic attack which takes place in phenazonium compounds (see following paper), but in

common with other pyrazine salts containing suitable saturated 1-substituents are decomposed by alkalis with the production of unsaturated bases.

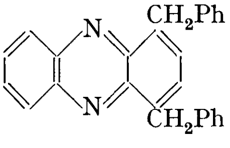
BENZALDEHYDE and 1 : 2 : 3 : 4-tetrahydrophenazine react on heating with the production of a *compound* $C_{26}H_{20}N_2$, which is considered to have the structure (III) rather than (II) [compare the production of the distyrylquinoxaline (I) by Bennett and Willis, J., 1928, 1960] on account of its resistance to oxidation and dehydrogenation. *p*-Nitrobenzaldehyde also reacts with the tetrahydrophenazine, in acetic anhydride solution, with the production of 1-p-*nitrobenzyl*-3 : 4-*dihydrophenazine* (IV, R = NO_2) and 1 : 4-*bis*-p-*nitrobenzylphenazine* (V, R = NO_2), separable by the greater basicity and solubility of the former compound.



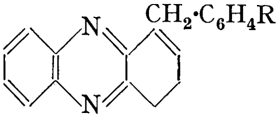
(I.)



(II.)



(III.)



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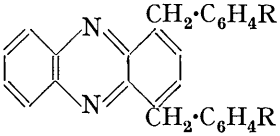
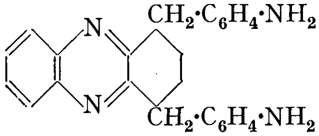


(V.)

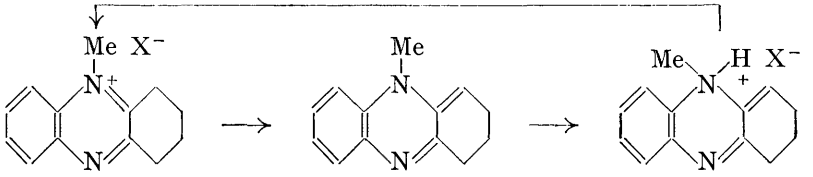


(VI.)

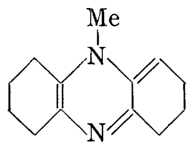
1-Aminophenazine derivatives may be of pharmacological interest (compare the acridine series; Mauss and Mietzsch, *Klin. Woch.*, 1933, 12, 1276), and it was attempted to prepare such compounds by these methods; direct condensation did not, however, take place between 1 : 2 : 3 : 4-tetrahydrophenazine and *p*-nitrosodimethylaniline, and 1 : 2 : 3 : 4-tetrahydrophenazine methiodide decomposed during the reaction. Production of an amine from the bis-*p*-nitrobenzylphenazine (V, R = NO_2) was accompanied by reduction of the nucleus, yielding 1 : 4-*bis*-p-*aminobenzyl*-1 : 2 : 3 : 4-*tetrahydrophenazine* (VI), but aminobenzylphenazines were prepared by condensation of *p*-dimethylaminobenzaldehyde with tetrahydrophenazine: refluxing in acetic anhydride solution produced 1-p-*dimethylaminobenzyl*-3 : 4-*dihydrophenazine* (IV, R = NMe_2) or 1 : 4-*bis*-p-*dimethylaminobenzylphenazine* (V, R = NMe_2) according to the proportions of reactants and the time of heating.

All the dibenzylphenazines prepared were slightly soluble in the commoner organic solvents, forming yellow fluorescent solutions, and yielded addition compounds with ferric chloride in glacial acetic acid.

The ready decomposition of 1 : 2 : 3 : 4-tetrahydrophenazine methiodide, which occurred with loss of halogen, led to an investigation of the action of alkali on the salt. The product of this reaction was a yellow oil, soluble in ether and benzene, which distilled unchanged under reduced pressure. This was clearly not the ammonium hydroxide and analysis indicated that it was not a *ψ*-base, but was produced from the hydroxide by loss of water.



(VII.) (VIII.) (IX.)



(X.)

1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-*Octahydrophenazine methiodide* similarly produced a dehydro-base, obtained as a yellow oil, b. p. 160°/1 mm. The absence of an analogous reaction in pyrazine methiodide indicates that the change involves one of the hydrogen atoms of the reduced phenazine nucleus, and it is suggested that it follows the course indicated in (VIII) and (X).

The action of acids on the N-*methyltetrahydrophenazine* (VIII) produced first an unstable red salt, which changed spontaneously in the course of a few minutes to a normal yellow tetrahydrophenazonium salt; this is presumably the isomerisation (IX) to (VII) in the above scheme. The N-*methyloctahydrophenazine* (X) reacts in the same way, and these changes are also paralleled by those investigated in the methylpyrazines by Gastaldi (*Gazzetta*, 1929, **59**, 751) and by Aston (*J. Amer. Chem. Soc.*, 1931, **53**, 1448). The dehydro-bases were also the only isolable products from the action of sodium cyanide, sulphite, and sulphide on the methiodides of the tetrahydro- and octahydro-phenazines.

EXPERIMENTAL.

1 : 4-*Dibenzylphenazine*.—1 : 2 : 3 : 4-Tetrahydrophenazine (J., 1934, 1991) (3 g.) and freshly distilled benzaldehyde (4 g.) were heated at 200° for 30 minutes; water was evolved during the first 10 minutes and, on cooling, the material set to a resin, which crystallised from alcohol or benzene–alcohol (1 : 2) in sulphur-yellow needles, m. p. 158° (Found: C, 87·1; H, 5·8. $C_{26}H_{20}N_2$ requires C, 86·7; H, 5·6%). The compound was not dehydrogenated by the action of iodine in glacial acetic acid, potassium ferricyanide, or by sulphur and selenium in xylene. Ferric chloride in glacial acetic acid produced a solvated *ferrichloride*, crystallising in large blood-red prisms, m. p. 200° (Found : C, 57·6; H, 4·1; residue, 13·4. $C_{26}H_{20}N_2,FeCl_3,C_2H_4O_2$ requires C, 57·7; H, 4·1; residue, 13·7%); its solutions in acetic acid were deep red, but in alcohol and ether were yellow, and from them, on concentration, 1 : 4-*dibenzylphenazine* separated. The salt also decomposed in water.

1-p-*Nitrobenzyl*-3 : 4-*dihydrophenazine and* 1 : 4-*Bis*-p-*nitrobenzylphenazine*.—1 : 2 : 3 : 4-Tetrahydrophenazine (1·8 g.), *p*-nitrobenzaldehyde (3·5 g.), and acetic anhydride (15 c.c.) were refluxed for 40 minutes; a bulky precipitate separated before or during cooling, and was filtered off immediately, washed with alcohol, and recrystallised from benzene or chloroform. It formed yellow plates (2·4 g.), m. p. 250°, whose analysis (Found : C, 69·7; H, 4·1. $C_{26}H_{18}O_4N_4$ requires C, 69·4; H, 4·0%) indicated it to be the 1 : 4-*bis*-p-*nitrobenzyl* compound.

From the acetic acid mother-liquors, after 24 hours, a material (0·9 g.) separated, which crystallised from alcohol in yellow prisms, m. p. 172°, and analysis (Found : C, 72·1; H, 5·0. $C_{19}H_{15}O_2N_3$ requires C, 71·9; H, 4·7%) showed it to be the product of an equimolecular condensation. It differed from the dibenzyl compound in forming a rich red solution in concentrated hydrochloric acid (that of the dibenzyl compound is yellow) and in being soluble in dilute acids.

1 : 4-*Bis*-p-*aminobenzyl*-1 : 2 : 3 : 4-*tetrahydrophenazine*.—The preceding dinitro-compound (0·4 g.), concentrated hydrochloric acid (20 c.c.), and stannous chloride (10 g.) were warmed at 100° for 2 hours; the initially red solution became green and then red again. Water was added, the solution basified (sodium hydroxide) and extracted with ether, the extract dried, the solvent removed, and the residue crystallised from alcohol, yielding colourless plates, m. p. 176° (Found: C, 78·9; H, 6·8. $C_{26}H_{26}N_4$ requires C, 79·2; H, 6·6%). It yielded a diazonium compound, but gave no coloration with ferric chloride (*i.e.*, is not reduced in the *NN'*-positions). Titanous chloride or hydrogen sulphide did not reduce the original dinitro-compound.

1-p-*Dimethylaminobenzyl*-3 : 4-*dihydrophenazine*.—1 : 2 : 3 : 4-Tetrahydrophenazine (1·0 g.), *p*-dimethylaminobenzaldehyde (1·6 g.), and acetic anhydride (10 c.c.) were refluxed for 40 minutes, the solution was warmed with water to decompose the anhydride, basified (sodium hydroxide), and extracted with ether, the extract dried, the solvent removed, and the residue crystallised from methyl alcohol and recrystallised from benzene, yielding yellow prisms of the equimolecular condensation *product* (0·5 g.), m. p. 158° (Found : C, 80·2; H, 6·9. $C_{21}H_{21}N_3$ requires C, 80·0; H, 6·7%).

1 : 4-*Bis*-p-*dimethylaminobenzylphenazine*.—The tetrahydrophenazine (0·5 g.), *p*-dimethylaminobenzaldehyde (2·0 g.), and acetic anhydride (10 c.c.) were refluxed for 6 hours; the product, separated as described above, crystallised from benzene in bright cinnabar-red prisms (0·2 g.), m. p. 207°, of the *bis*-p-*dimethylaminobenzyl* compound (Found: C, 80·5; H, 6·7. $C_{30}H_{30}N_4$ requires C, 80·7; H, 6·7%).

1 : 2 : 3 : 4-*Tetrahydrophenazine Monomethiodide*.—The base (4 g.) and methyl iodide (4 g.) were heated in a sealed tube at 100° for 2 hours, and the product washed with ether and crystallised from aqueous alcohol (6·4 g., m. p. 207°) (Found : I, 39·2. $C_{13}H_{15}N_2I$ requires I, 39·0%).

9-*Methyl*-2 : 3 : 4 : 9-*tetrahydrophenazine*.—An aqueous solution of 1 : 2 : 3 : 4-tetrahydrophenazine methiodide was basified (sodium hydroxide) and extracted with ether, and the extract concentrated and distilled in a vacuum, yielding the *base* as a viscous, golden-yellow oil, b. p. 170°/1 mm. (Found : C, 78·5; H, 7·2. $C_{13}H_{14}N_2$ requires C, 78·8; H, 7·1%). Qualitative tests indicated the base to be unchanged by distillation; it was volatile in steam and yielded indefinite salts with picric acid. In the air, the base was converted after a few days into a red tar; oxidising agents caused this change immediately. The base yielded phenazine (20%) when dehydrogenated with palladium–charcoal at 200°.

1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-*Octahydrophenazine Methiodide.*—The octahydro-compound (1·0 g.), freshly distilled methyl iodide (2·0 g.), and methyl alcohol (1·0 c.c.) were heated in a sealed tube at 100° for 6 hours; the *product* crystallised from water in yellow prisms, m. p. 175° (Found: I, 38·3. $C_{12}H_{16}N_2$,MeI requires I, 38·5%). The green-violet compound described by Godchot (*Compt. rend.*, 1925, **180**, 444) as *s*-octahydrophenazine methiodide must be regarded as impure.

9-*Methyl*-2 : 3 : 4 : 5 : 6 : 7 : 8 : 9-*octahydrophenazine.*—The above methiodide (2 g.) was dissolved in water (20 c.c.), sodium hydroxide solution added in excess, the mixture extracted with ether, and the extract dried; the *product* distilled under reduced pressure (b. p. 160°/1 mm.) as an orange-yellow oil (1 g.) (Found: C, 77·3; H, 8·9. $C_{13}H_{18}N_2$ requires C, 77·2; H, 8·9%), which rapidly turned red in air.

I wish to acknowledge my indebtedness to Professor G. R. Clemo for advice received, to Mr. O. Telfer for microanalyses, and to the Department of Scientific and Industrial Research for a maintenance grant and research award.

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[*Received, September 7th*, 1937.]