74. *Some Dichloro- and Dibromo-derivatives of* 1 : 2 : 3 : 4-*Tetrahydrophenazine and* cis-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*Octahydrophenazine.**

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It has been shown that whereas halogenation of 5-acetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine affords 6 : 8-dichloro- and 6 : 8-dibromo-compounds, 5 : 10-diacetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine is dibrominated in the 7- and the 8-position.

THEORETICAL considerations suggested that the compound $C_{16}H_{18}O_2N_2Br_2$, m. p. 202—204°, obtained[1] by bromination of *cis*-5 : 10-diacetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine (I; R = R′ = Ac; X = H) is most probably *cis*-5 : 10-diacetyl-7 : 8-dibromo-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine (I; R = R′ = Ac; X = Br); whereas the isomeric substance, m. p. 118—120°, obtained by bromination and subsequent acetylation of *cis*-5-acetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine (I; R = Ac; R′ = X = H) is 5 : 10-diacetyl-6 : 8-dibromo-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine † (II; R = R′ = Ac; X = Br). Synthesis of these two diacetyldibromo-octahydrophenazines has now proved that this is so.

Chlorination of the compound (I; R = R′ = Ac; X = H) did not afford crystalline material but when 5-acetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine was chlorinated

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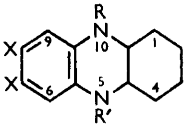
* The compounds described in *J.*, 1956, 794, are 1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine and its 9 : 10-derivatives, according to the numbering used in this paper.

† This and all other octahydrophenazines in this paper are presumably *cis*-compounds.

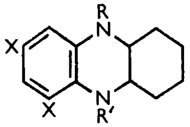
[1] Earle and Tomlinson, *J.*, 1956, 794.

in acetic acid it gave, after acetylation, a substance which has been identified as 5 : 10-diacetyl-6 : 8-dichloro-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine (II; R = R′ = Ac; X = Cl).

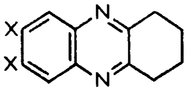
These dichloro- and dibromo-phenazines have been synthesised from the appropriate 1 : 2-diamino-dichloro- and -dibromo-benzene and 2-hydroxy*cyclo*hexanone. It was



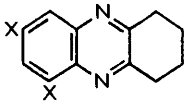
(I)



(II)



(III)



(IV)

shown[1] that when *o*-phenylenediamine is condensed with 2-hydroxy*cyclo*hexanone, equimolecular quantities of 1 : 2 : 3 : 4-tetrahydro- (III; X = H) and *cis*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydro-phenazine (II; R = R′ = X = H), compounds previously described by Clemo and McIlwain,[2, 3] are produced. With the dihalogeno-*ortho*-diamines used in this work, in only one instance, namely with 1 : 2-diamino-4 : 5-dichlorobenzene, were both the tetrahydro- (III; X = Cl) and the octahydro-phenazines (I; R = R′ = H; X = Cl) obtained. In all other cases the sole product was the dihalogenotetrahydrophenazine. These chloro- and bromo-tetrahydrophenazines are readily reduced catalytically to 1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine but carefully controlled hydrogenation, in the presence of acetic anhydride, affords monoacetyl derivatives of the corresponding dihalogeno-octahydro-compounds, and the monoacetyl compounds obtained in this way from 6 : 8-dichloro- (IV; X = Cl) and 6 : 8-dibromo-1 : 2 : 3 : 4-tetrahydrophenazine (IV; X = Br) were identical with those obtained by chlorination and bromination, respectively, of 5-acetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine. The position of the acetyl group here is not proved, but steric considerations leave little doubt that these compounds are 5-acetyl-6 : 8-dichloro- (II; R = Ac, R′ = H; X = Cl) and 5-acetyl-6 : 8-dibromo-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine (II; R = Ac; R′ = H; X = Br), respectively.

Of the diamines used here, the 3 : 5-dichloro- and 3 : 5-dibromo-compounds were prepared by catalytic reduction of the corresponding 2-nitro-amines; 1 : 2-diamino-4 : 5-dichlorobenzene was prepared from 1 : 2 : 4-trichlorobenzene,[4] while 1 : 2-diamino-4 : 5-dibromobenzene was obtained from 1 : 2-dibromobenzene by dinitration and subsequent reduction.[5]

EXPERIMENTAL

1 : 2-*Diamino*-3 : 5-*dichlorobenzene*.—4 : 6-Dichloro-2-nitroaniline (20 g.) [prepared by chlorinating *o*-nitroaniline in acetic acid (compare Holleman and van Haeften [6])] in tetrahydrofuran (60 c.c.) was hydrogenated over Raney nickel at 5 atm. and room temperature, until the solution became colourless. Dilution with water, after removal of the catalyst, yielded a solid (10 g.) which crystallised from alcohol to give 1 : 2-diamino-3 : 5-dichlorobenzene as needles, m. p. 60—61°. 1 : 2-Diamino-3 : 5-dibromobenzene (12 g.), needles, m. p. 83°, was similarly prepared from the nitro-compound (15 g.).

1 : 2-*Diamino*-4 : 5-*dibromobenzene*.—1 : 2-Dibromo-4 : 5-dinitrobenzene (2 g.) and stannous chloride (11·6 g.) were mixed and added slowly to hydrochloric acid (50 c.c.). The mixture was stirred at 100° until it became colourless, and the solid was collected and decomposed with sodium hydroxide. The precipitated diamine crystallised from alcohol as needles, m. p. 155° (sintering at 140°) (Found: C, 27·5; H, 2·5. Calc. for $C_6H_6N_2Br_2$: C, 27·1; H, 2·3%). Schiff [5] gives m. p. 137°.

[2] Clemo and McIlwain, *J.*, 1934, 1991.
[3] *Idem, J.*, 1936, 259.
[4] Acheson, Taylor, and Tomlinson, *J.*, 1958, 3750.
[5] Schiff, *Monatsh.*, 1890, **11**, 338.
[6] Holleman and van Haeften, *Rec. Trav. chim.*, 1921, **40**, 67.

Condensation of 1 : 2-*Diamino*-4 : 5-*dichlorobenzene with* 2-*Hydroxy*cyclo*hexanone.*—1 : 2-Diamino-4 : 5-dichlorobenzene (6 g.) and 2-hydroxy*cyclo*hexanone (4·2 g.) were powdered together and heated at 140° until evolution of water vapour ceased. The mass solidified and was recrystallised from alcohol from which separated 7 : 8-*dichloro*-1 : 2 : 3 : 4-*tetrahydrophenazine* (3·5 g.) as needles, m. p. 183·5° (Found: C, 57·2; H, 4·1. $C_{12}H_{10}N_2Cl_2$ requires C, 56·9; H, 4·0%). Concentration of the mother liquor to half-bulk afforded needles (3 g.), which on further recrystallisation from alcohol gave 7 : 8-*dichloro*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine*, m. p. 152° (Found: C, 56·3; H, 5·2. $C_{12}H_{14}N_2Cl_2$ requires C, 56·0; H, 5·5%).

5-*Acetyl*-7 : 8-*dichloro*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine.*—A solution of 7 : 8-dichloro-1 : 2 : 3 : 4-tetrahydrophenazine (2·39 g.) in acetic acid (130 c.c.) and acetic anhydride (20 c.c.) was warmed with a little palladium–charcoal and then filtered and hydrogenated over fresh catalyst (0·3 g.; 10% Pd) until hydrogen (466 c.c. at 16·5° and 741 mm.) had been absorbed. Dilution with aqueous potassium acetate precipitated 5-*acetyl*-7 : 8-*dichloro*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine* which crystallised from alcohol as needles, m. p. 216° (Found: C, 56·5; H, 5·2. $C_{14}H_{16}ON_2Cl_2$ requires C, 56·2; H, 5·3%).

5 : 10-*Diacetyl*-7 : 8-*dichloro*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine.*—This was obtained when the above octahydro-compound or its 9-acetyl derivative was boiled with acetic anhydride (20 min.). It separated from alcohol as needles, m. p. 166—167° (Found: C, 56·0; H, 5·5. $C_{16}H_{18}O_2N_2Cl_2$ requires C, 56·3; H, 5·3%).

7 : 8-*Dibromo*-1 : 2 : 3 : 4-*tetrahydrophenazime.*—Condensation of 1 : 2-diamino-4 : 5-dibromobenzene (10·3 g.) with 2-hydroxy*cyclo*hexanone (4·3 g.) at 110—130° (30 min.) gave a brown mass which crystallised (6·8 g.) on trituration with alcohol. Recrystallisation from light petroleum (b. p. 60—80°) gave 7 : 8-*dibromo*-1 : 2 : 3 : 4-*tetrahydrophenazine* as needles, m. p. 188·5° (Found: C, 42·2; H, 2·9. $C_{12}H_{10}N_2Br_2$ requires C, 42·1; H, 2·9%). Attempts to isolate the octahydro-compound or an acetyl derivative of it from the mother liquor were unsuccessful.

5-*Acetyl*-7 : 8-*dibromo*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine.*—This was prepared by reductive acetylation (as above) of the tetrahydro-compound (0·83 g.). Hydrogen (115 c.c. at 18·5° and 754 mm.) was absorbed, and addition of aqueous ammonia precipitated 5-*acetyl*-7 : 8-*dibromo*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine* which crystallised as prisms, m. p. 190—192° (Found: C, 43·7; H, 4·2. $C_{14}H_{16}ON_2Br_2$ requires C, 43·3; H, 4·1%).

5 : 10-*Diacetyl*-7 : 8-*dibromo*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine.*—When the solution from the above hydrogenation was boiled for 20 min. and then neutralised with aqueous ammonia, 5 : 10-diacetyl-7 : 8-dibromo-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine was obtained, m. p. 202—204° (from alcohol) not depressed by admixture with the compound, m. p. 202—204°, obtained by bromination of 5 : 10-diacetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine.

6 : 8-*Dichloro*-1 : 2 : 3 : 4-*tetrahydrophenazine.*—1 : 2-Diamino-3 : 5-dichlorobenzene (1·7 g.) and 2-hydroxy*cyclo*hexanone (1·13 g.) were condensed at 120°. The product crystallised in contact with alcohol and was recrystallised from alcohol giving 6 : 8-*dichloro*-1 : 2 : 3 : 4-*tetrahydrophenazine*, m. p. 116—116·5° (Found: C, 56·7; H, 3·9. $C_{12}H_{10}N_2Cl_2$ requires C, 56·9; H, 3·9%). No octahydro-compound could be isolated.

5-*Acetyl*-6 : 8-*dichloro*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine.*—(*a*) On reductive acetylation (as above) 6 : 8-dichloro-1 : 2 : 3 : 4-tetrahydrophenazine (1·1 g.) absorbed hydrogen (206 c.c. at 14° and 755 mm.) giving 5-*acetyl*-6 : 8-*dichloro*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine*, plates, m. p. 132—133° (from alcohol).

(*b*) A solution of chlorine (3·7 g.) in acetic acid was added to 5-acetyl-1:2:3:4:5:10:11:12-octahydrophenazine (6 g.) also in acetic acid. The mixture was immediately diluted with water, and the gummy precipitate was redissolved in acetic acid and precipitated again. It then crystallised from alcohol as plates, m. p. 130—132° (3·3 g.), identical (mixed m. p.) with the above substance (Found: C, 56·8; H, 5·4; N, 9·5. $C_{14}H_{14}ON_2Cl_2$ requires C, 56·2; H, 5·4; N, 9·4%). When this was boiled with acetic anhydride and a trace of sulphuric acid it gave 5 : 10-*diacetyl*-6 : 8-*dichloro*-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-*octahydrophenazine*, plates (from alcohol), m. p. 132·5—133·5° depressed by admixture with the above (Found: C, 56·2; H, 5·3; N, 8·1. $C_{16}H_{18}O_2N_2Cl_2$ requires C, 56·3; H, 5·3; N, 8·2%).

6 : 8-*Dibromo*-1 : 2 : 3 : 4-*tetrahydrophenazine.*—1 : 2-Diamino-3 : 5-dibromobenzene (30 g.) and 2-hydroxy*cyclo*hexanone (12·4 g.) condensed at 110—130° (20 min.) gave 6 : 8-*dibromo*-1 : 2 : 3 : 4-*tetrahydrophenazine* (17·9 g.), needles, m. p. 105° (from alcohol) (Found: C, 42·3;

H, 3·1; N, 8·0. $C_{12}H_{10}N_2Br_2$ requires C, 42·1; H, 2·9; N, 8·2%): on reductive acetylation this tetrahydro-compound (2·47 g.) in acetic acid (150 c.c.) and acetic anhydride (20 c.c.) absorbed hydrogen (370 c.c. at 14° and 748 mm.) to give 5-acetyl-6 : 8-dibromo-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine, m. p. 117—118°; the m. p. was slightly raised on admixture with the compound, m. p. 118—119°, prepared by bromination of 9-acetyl-octahydrophenazine. 5 : 10-Diacetyl-6 : 8-dibromo-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine was obtained from this by further acetylation, and its m. p. 164·5° was not depressed by admixture with the diacetyl compound, m. p. 164—165°, prepared by brominating and acetylating 5-acetyl-1 : 2 : 3 : 4 : 5 : 10 : 11 : 12-octahydrophenazine.

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