

## 55. The Phenazine Series. Part III. The Isomeric Octahydrophenazines.

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IN preparing a considerable quantity of 1 : 2 : 3 : 4-tetrahydrophenazine (J., 1934, 1991), we isolated a small amount of an *octahydrophenazine*, m. p. 147°, as a by-product. We have recorded (J., 1935, 738) the production of a 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenazine, m. p. 156° (there given in error as 150°), by the sodium amalgam reduction of the tetrahydro-compound. The following results prove these two compounds to be geometrical and not structural isomerides: both are dehydrogenated smoothly to phenazine; both yield *N-nitroso*-compounds (m. p. 109° and 126°), from which it follows that the central heterocyclic ring is in each case reduced, as in (I); and both give the ferric chloride colour reactions characteristic of substituted *o*-phenylenediamines.



In addition, by the reduction of 1 : 2 : 3 : 4-tetrahydrophenazine by a nickel catalyst *A* made from nickel nitrate according to Gattermann ("Laboratory Methods of Organic Chemistry," English edition, 1934, p. 370), a third octahydrophenazine, m. p. 109°, is obtained, which also is dehydrogenated to phenazine, but yields no nitroso-compound or ferric chloride colour reaction. It is therefore the 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydrophenazine (II) described by Wallach (*Annalen*, 1924, 437, 177) and by Godchot (*Compt. rend.*, 1925, 180, 444). On theoretical grounds, (II) would not be expected to exist in isomeric forms. The isomeric 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenazines are, however, produced from the tetrahydro-compound by reduction with a nickel catalyst *B* prepared from nickel hydroxide (Rupe, *Helv. Chim. Acta*, 1918, 1, 453); in the vapour phase at 180°, the main product is the compound of m. p. 156°, but in glacial acetic acid at room temperature the 147°-isomeride is produced. The actions of the two catalysts are different, for when either of the two compounds (I) is passed over catalyst *A* it is

converted into the isomeride (II); the latter is, however, recovered unchanged after passage over catalyst *B*. We do not know of any other case in which the use of the two catalysts has caused radically different reductions; it is noteworthy, however, that they are of different physical appearance.

Though the octahydrophenazine isolated as a by-product in the preparation of tetrahydrophenazine from *o*-phenylenediamine and *cyclohexane-1:2-dione* is presumably produced on account of the reducing action of one or both of these reactants, it has not been found possible to reduce tetrahydrophenazine to the octahydro-compound by treating it with the diamine or the diketone under the conditions of the reaction (*loc. cit.*), which indicates that the reduction leading to the production of the octahydrophenazine must have occurred before or during the condensation.

In addition to the nickel reduction mentioned above, it is possible to reduce the tetrahydrophenazine almost quantitatively to the octahydrophenazine of *m. p.* 147° by means of palladium charcoal in glacial acetic acid. The following table summarises the various reduction results:

Initial material.	Reducing agent.	Product.
1 : 2 : 3 : 4 - Tetrahydrophenazine	(a) Sodium-alcohol	1 : 2 : 3 : 4 : 9 : 10 : 11 : 12 - Octahydrophenazine, <i>m. p.</i> 156°
	(b) Pt or Pd; or Ni [from Ni(OH) <sub>2</sub> ] in glacial acetic acid	1 : 2 : 3 : 4 : 9 : 10 : 11 : 12 - Octahydrophenazine, <i>m. p.</i> 147°
	(c) Ni [from Ni(NO <sub>2</sub> ) <sub>2</sub> ] at 180°	1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 - Octahydrophenazine
	(d) Ni [from Ni(OH) <sub>2</sub> ] at 180°	1 : 2 : 3 : 4 : 9 : 10 : 11 : 12 - Octahydrophenazine, <i>m. p.</i> 156°, with a little of its 147°-isomeride.
1 : 2 : 3 : 4 : 9 : 10 : 11 : 12 - Octahydrophenazine, <i>m. p.</i> 156°	(a) Sodium-alcohol; H <sub>2</sub> with Pd in acetic acid; Ni [from Ni(OH) <sub>2</sub> ] at 180°	No change
	(b) Ni [from Ni(NO <sub>2</sub> ) <sub>2</sub> ] at 180°	1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 - Octahydrophenazine
1 : 2 : 3 : 4 : 9 : 10 : 11 : 12 - Octahydrophenazine, <i>m. p.</i> 147°	(a) Sodium-alcohol; H <sub>2</sub> with Pd in acetic acid	No change.
	(b) Ni [from Ni(NO <sub>2</sub> ) <sub>2</sub> ] at 180°	1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 - Octahydrophenazine
	(c) Ni [from Ni(OH) <sub>2</sub> ] at 180°	Partly converted into 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12 - octahydrophenazine, <i>m. p.</i> 156°

The most suitable method of dehydrogenating the reduced phenazines described here has been found to be  $\frac{1}{2}$  hour's heating at 200° with palladium charcoal; it is much superior to the iodine method employed for the preparation of phenazine and its homologues from their 1 : 2 : 3 : 4-tetrahydro-forms (J., 1934, 1991) and to the zinc dust distillation used by Godchot (*loc. cit.*) for the conversion of a duododecahydrophenazine into phenazine.

It has not been found possible to interconvert the *cis-trans* forms of 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenazine by refluxing with glacial acetic acid, or sodium ethoxide, or by keeping their concentrated sulphuric acid solutions for considerable periods; but the 147°-isomeride is converted into the 156°-compound by passage in a hydrogen stream over catalyst *B*. With respect to the configurations of these two isomerides, their methods of production point to the 147°-compound being the *cis*- and the 156°-compound the *trans*-isomeride (compare Willstätter and Seitz, *Ber.*, 1924, 57, 683; W. Hüchel, *Annalen*, 1926, 451, 109, 132). The latter should be resolvable into optically active forms.

It is hoped that the study, now in progress, of the fully reduced phenazines will afford further evidence on this question, and also add knowledge to the increasingly important question of the stereochemistry of polycyclic compounds.

#### EXPERIMENTAL.

1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-Octahydrophenazine, *m. p.* 156° (see J., 1935, 738).—A much improved method is the following: To a solution of 1 : 2 : 3 : 4-tetrahydrophenazine (1.8 g.)

in absolute alcohol (75 c.c.) boiling under reflux, sodium (10 g.) was added gradually; the yellow solution became colourless, and when the reaction was complete it was poured into water (150 c.c.) and extracted with ether. The residue on removal of ether was repeatedly crystallised from alcohol, yielding the 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenazine in white needles (1.4 g.). The action of sodium in amyl-alcoholic solution was essentially the same, and a larger excess of sodium produced no different result.

1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-Octahydrophenazine, *m. p.* 147°.—1 : 2 : 3 : 4-Tetrahydrophenazine (1 g.) in absolute alcohol (10 c.c.) with palladium charcoal (0.1 g.) was shaken vigorously for 20 hours in a hydrogen atmosphere of 100 lb. per sq. in. The catalyst was removed and when the filtrate was concentrated the bulk of the octahydrophenazine separated in colourless plates (0.9 g.), *m. p.* 147°, depressed to 122—124° by admixture with the 156°-isomeride (Found : C, 76.8; H, 8.8.  $C_{12}H_{16}N_2$  requires C, 76.6; H, 8.5%).

Reduction of the same amount of tetrahydro-compound in glacial acetic acid (10 c.c.) with nickel catalyst *B* (1 g.) under the above conditions for 12 hours yielded the same product (0.8 g.). The same material (0.5 g.) was also obtained during the crystallisation of tetrahydrophenazine (40 g.) (*loc. cit.*) from light petroleum.

No molecular compound or complex salt was obtained between this octahydrophenazine and phenazine when examined by the methods previously described (J., 1935, 738).

*Catalytic Reductions with Nickel.*—The following method was devised for the reduction of small amounts of not very volatile materials. A slightly inclined, hard-glass tube, 16"  $\times$  ½", contained a 10" column of the catalyst, held between asbestos plugs and heated by a small gas furnace fitted with a thermometer. The material to be reduced was placed in a boat in the upper part of the tube and was driven over the catalyst in a stream of hydrogen by heating a gauze surrounding the tube at that point. The hydrogen (from zinc and hydrochloric acid) was washed in silver nitrate solution, alkaline permanganate solution, and concentrated sulphuric acid, and at the exit end of the tube it was passed through a trap containing alcohol.

The nickel catalyst *A* was prepared from the nitrate by the method of Gatterman (*loc. cit.*) and reduced at 300—310° for 2 hours, and catalyst *B* from nickel hydroxide by a 48 hours' reduction at 370—380° (Rupe, *loc. cit.*). The hydrogenations were performed at 175—185° and required about 6 hours. The catalyst (about 20 g.) was reduced in a hydrogen stream of 50 c.c. per minute while the gas was being actively absorbed; the rate was later diminished to 15 c.c. per minute. The hydrogenations were conducted in a stream of 40 c.c. per minute.

*Hydrogenation of 1 : 2 : 3 : 4-tetrahydrophenazine.* (i) *With catalyst A.* The compound (1 g.) was passed through the apparatus just described; extraction of the catalyst and crystallisation from dilute alcohol yielded an octahydrophenazine (0.5 g.), *m. p.* 109° (Found : C, 76.7; H, 8.55. Calc. for  $C_{12}H_{16}N_2$  : C, 76.6; H, 8.5%).

(ii) *With catalyst B.* The product from tetrahydrophenazine (1 g.), when crystallised from light petroleum, yielded 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenazine (0.4 g.), *m. p.* 156° (not depressed by admixture with the product of the sodium-alcohol reduction of the tetrahydro-compound), recovered tetrahydrophenazine (0.3 g.), and a fraction (0.2 g.), *m. p.* 122—124°, which on further laborious fractionation from light petroleum or, better, from benzene yielded some octahydrophenazine, *m. p.* 156°, though the bulk still melted at 123—124°. The analysis (Found : C, 77.0; H, 8.4. Calc. for  $C_{12}H_{16}N_2$  : C, 76.6; H, 8.5%) indicated that no further-reduced compound was present in the bulk; though we were unable to separate it completely, this probably consisted of mixed crystals of the two 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenazines, for when these two compounds were crystallised together they yielded a fraction which after repeated crystallisation melted at 123—124°. A further passage of this material over the same catalyst enabled more of the 156°-isomeride to be obtained from it.

*The action of hydrogen on the isomeric octahydrophenazines under the influence of catalysts A and B.* (i) *Isomeride, m. p.* 156°, *with catalyst A.* The compound (1 g.), when passed once through the furnace, yielded 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydrophenazine (0.5 g., from dilute alcohol), and 0.4 g. of the initial material was recovered. A more complete conversion was obtained on repressing the material under the same conditions.

(ii) *Isomeride, m. p.* 156°, *with catalyst B.* The bulk of the material was recovered unchanged, but a small fraction (0.1 g. from 2 g.) was obtained, *m. p.* 120—124°, which proved to be a mixture of the type described above.

(iii) *Isomeride, m. p.* 147°, *with catalyst A.* The product from the passage of 1 g. was crystallised from alcohol and yielded recovered material (0.3 g.); the mother-liquors were diluted with water, and further crystallisation gave 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydrophenazine (0.5 g.).

(iv) *Isomeride, m. p.* 147°, *with catalyst B.* The bulk of the product, collected as before,

melted at 120—124°, and proved to be a mixture of the two 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenazine isomerides. A more complete conversion into the 156°-isomeride was obtained on repassage.

(v) *Isomeride, m. p.* 109°, *with catalysts A and B.* No change occurred after three passages under the above conditions.

*Nitroso-compounds of the Reduced Phenazines (I).*—0.1 G. was dissolved in dilute sulphuric acid (5 c.c.), and sodium nitrite (0.1 g.) added; after a few minutes, excess of urea was added, and the product extracted with ether; this was dried, and removed under reduced pressure at room temperature, as warming caused decomposition. The product was crystallised from alcohol. 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-Octahydrophenazine, *m. p.* 156°, thus yielded a *dinitroso*-compound, *m. p.* 126° (Found : C, 58.55; H, 5.7.  $C_{12}H_{14}O_2N_4$  requires C, 58.6; H, 5.7%); and 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenazine, *m. p.* 147°, a *dinitroso*-compound, *m. p.* 109° (Found : C, 58.3; H, 5.8%).

*Dehydrogenation of the Octahydrophenazines with Palladium Charcoal.*—Each of the three compounds (0.1 g.) was independently mixed with palladium charcoal (0.05 g.) in a small, loosely stoppered tube and heated in an oil-bath at 200° for  $\frac{1}{2}$  hour. A yellow sublimate of phenazine was obtained (about 0.06 g.), *m. p.* 171°, after crystallisation from light petroleum. Tetrahydrophenazine was similarly dehydrogenated.

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