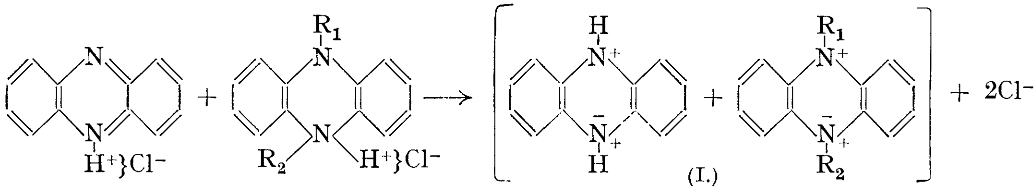
165. *Syntheses and Molecular Complexes in the Phenazine Series. Part II.*

By George R. Clemo and Henry McIlwain.

Though Briegleb (*Z. physikal. Chem.*, 1932, *B*, **16**, 249) has classified the types of linkage which can lead theoretically to molecular compounds, it is not easy to discriminate between these in practice, and there are few such compounds for which a single formula is generally accepted. We have suggested (Part I; J., 1934, 1991) a formula for the phenazhydrins formed from the phenazine and its reduced form involving the co-ordination of the nitrogen atom of the former with the imino-hydrogen atom of the latter. Though the conception of →H— may receive a different interpretation on current wave-mechanical views, there is chemical and physical evidence (see especially Sidgwick, *Ann. Reports*, 1934, 40) indicating that hydrogen has peculiar combining powers when joined to an atom of considerable " residual affinity " and that it can form a bridge between two such centres.

We have attempted to find the centres participating in complex formation in the phenazine series by varying the components. There appear to be two distinct types of molecular compound in the phenazine series: (1) The true phenazhydrins, formed between a phenazine and a 9 : 10-dihydrophenazine; these are much less soluble than their components in such solvents as alcohol or petrol, are green to purple, and form green dihydrochlorides. (2) Phenazine–primary or secondary aromatic base complexes; these are more soluble than the phenazhydrins, are orange-red, and do not give complex hydrochlorides.

A reason for the complex hydrochlorides being specific of the phenazhydrins proper is to be seen in Michaelis's formulation of these salts (*J. Amer. Chem. Soc.*, 1933, **55,** 1481),



(I.)

which he suggests owe their stability and colour to their existence as ions (I, $R_1 = R_2 = H$) (the monohydrochloride of phenazine is known; the *dihydrophenazine salt*, not previously described, has been found also to be a monohydrochloride). Evidence supporting this formulation has been obtained from a study of the methylated dihydrophenazines. *N*-Methyldihydrophenazine was made by the method of Hantzsch (*Ber.*, 1916, **49**, 513) through phenazine methosulphate; but *NN'*-dimethyldihydrophenazine could not be made similarly, as phenazine forms only a monomethosulphate. An intermolecular Ullmann reaction with *o*-chloro-*N*-methylaniline, which would have yielded the required compound, did not take place. It has been prepared, however, from *NN'*-dimethyl-*o*-phenylenediamine and *cyclo*hexane-1 : 2-dione by condensation and oxidation.

Neither of these methylated dihydrophenazines yields a complex with phenazine, thus supporting the formula II (Part I) for the phenazhydrins, but both form complex hydrochlorides, which can be written as (I : *a*, $R_1 = H$, $R_2 = CH_3$; *b*, $R_1 = R_2 = CH_3$).

Further evidence that the *N*-hydrogen atoms perform a function in complex formation which an *N*-methyl group cannot is furnished by the second class of phenazine molecular compounds: phenazine forms with diphenylamine a loosely-bound orange-coloured *complex* in the molecular ratio of 1 : 2; no combination was found with methyldiphenylamine. Phenazine and *o*-phenylenediamine form a 1 : 1-*complex*, but *NN'*-dimethyl-*o*-phenylenediamine does not combine, a result unexpected till one considers that mutual repulsion or steric interference of the two methyl groups will orient them, and consequently the *N*-hydrogen atoms, on opposite sides of the plane of the benzene ring.

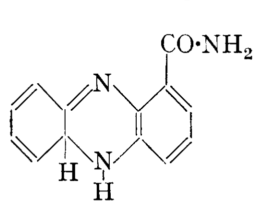
The nature of the complexes formed between phenazine and the various phenylenediamines indicates that an approach in space of the participating N and H atoms is necessary: with the *o*- and *m*-compounds, 1 : 1 complexes are formed, but under the same conditions the *p*-diamine yields a 1 : 2-*complex*. This supports the previously recorded observations on heteronuclear phenazhydrins (Part I). It is noteworthy that Buehler and collaborators (*J. Amer. Chem. Soc.*, 1932, **54**, 2398), from a physical study of the phenol–amines, concludes that these compounds also are bound co-ordinately.

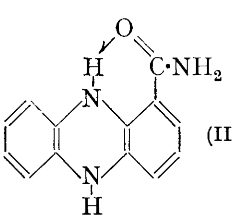
1 : 2 : 3 : 4-Tetrahydrophenazine, which contains the quinoxaline nucleus, has not been found to combine with dihydrophenazine; nor will 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenazine*, which contains two cyclic imino-groups between one benzenoid and one reduced ring, combine with phenazine or its tetrahydro-compounds. No complex is formed between the octahydro- and the tetrahydro-phenazine, nor between these compounds and diphenylamine. This indicates that the benzene nuclei also play some specific part, sterically or electromerically, in phenazhydrin formation.

Neither carbazole nor acridine gives complexes comparable with the phenazhydrins, but the latter does yield equimolecular compounds with such bases as diphenylamine (Blum, *Ber.*, 1929, **62**, 885).

Kögl and collaborators (*Annalen*, 1932, **497**, 266) consider that the reduced nucleus in the phenazhydrin chlororaphin is in the 10 : 13-dihydro-form (II). Their evidence—that chlororaphin has three active hydrogen atoms in its molecule, phenazine none, dihydrophenazine two, the amide of phenazine-α-carboxylic acid one, and hence the amide of 9 : 10-dihydrophenazine-α-carboxylic acid three, whereas in the form (II) it would have two such atoms, making with that of the amide of phenazine-α-carboxylic acid the observed three—can be criticised on two grounds.

(II.)





(III.)

We have found that chlororaphin gives in the amyl ether of a Zerewitinov estimation a yellow solution, taken by Kögl as signifying dissociation; he is thus estimating the active hydrogen atoms of a mixture of the amide of phenazine-α-carboxylic acid and its dihydro-form, which implies that the latter has two such atoms. We suggest that this discrepancy from the computed value is due to the co-ordination indicated in formula (III) and not to a radically different ring structure. Such co-ordination also explains the relative stability to oxidation exhibited by chlororaphin in comparison with the corresponding complex from the β-amide, the dihydro-form of which cannot so co-ordinate. Phenazine-β-carboxylic acid has been made in a similar manner to the α-acid (compare Part I) from 2-methylphenazine, and the latter from the two new *2-methyl* -1 : 2 : 3 : 4- and -5 : 6 : 7 : 8-*tetrahydrophenazines* described in the experimental part.

It was found that the β-amide would not yield the corresponding phenazhydrin by a simple zinc reduction as will the α-compound, and that when prepared from its 9 : 10-dihydro-form it oxidises in air at room temperature, whereas chlororaphin remains unchanged.

EXPERIMENTAL.

*Phenazine–*N*-methyldihydrophenazine Dihydrochloride.*—To a solution of *N*-methyldihydrophenazine (0·1 g.) and phenazine (0·1 g.) in the least amount of alcohol, saturated alcoholic hydrogen chloride (1 c.c.) was added; the *salt* precipitated from the dark green solution by ether crystallised from alcohol in fine green needles, m. p. 225° (approx., decomp.) (Found: Cl, 15·7, 16·0. $C_{12}H_8N_2,C_{13}H_{12}N_2,2HCl$ requires Cl, 15·8%). The salt yields with alkalis a mixture of its constituent bases, which form no compound in the usual solvents.

NN'*-Dimethyl-*2 : 3 : 9 : 10*-tetrahydrophenazine.*—*cyclo*Hexane-1 : 2-dione (5·6 g.), *NN'*-dimethyl-*o*-phenylenediamine (6·8 g.), and concentrated hydrochloric acid (20 c.c.) in water (60 c.c.) were rapidly brought to boiling, refluxed for 5 minutes, and quickly cooled, the hydrochloride of the condensation product was filtered off and dissolved in water, excess of sodium hydroxide added, and the *base* collected, washed with water, and crystallised from alcohol, forming colourless plates (2·2 g.), m. p. 78° (Found: C, 79·2; H, 7·85. $C_{14}H_{16}N_2$ requires C, 79·25; H, 7·6%).

NN'*-Dimethyl-*9 : 10*-dihydrophenazine.*—*cyclo*Hexane-1 : 2-dione (1 g.), *NN'*-dimethyl-*o*-phenylenediamine (1·2 g.), sodium acetate (2 g.), and glacial acetic acid (5 c.c.) were refluxed for 40 minutes and poured into water and the mixture was made alkaline and extracted with ether. From the resinous ethereal concentrates, a *solid* (0·15 g.) was separated with difficulty, and crystallised from benzene or absolute alcohol in almost colourless prisms, m. p. 153° (Found: C, 80·1; H, 6·65; N, 13·2. $C_{14}H_{14}N_2$ requires C, 80·0; H, 6·7; N, 13·3%).

This substance was also produced when solutions of the above tetrahydro-compound were exposed to the air for some days, or an acetic acid solution was warmed in the open for ½ hour; the bulk of the material was, however, converted into a resin, and the usual dehydrogenating agents gave no better yield. The colourless hydrochloride of *NN'*-dimethyldihydrophenazine turned green on exposure to air or on the addition of oxidising agents; when an oxidised solution was made alkaline and extracted with light petroleum, phenazine was obtained. A similar oxidative demethylation was observed with *N*-methyldihydrophenazine.

*Phenazine–*NN'*-dimethyl-*9 : 10*-dihydrophenazine Dihydrochloride.*—The *salt* was obtained, in the same way as its monomethyl analogue above, in dark green needles, m. p. 225—230° (decomp.) (Found: Cl, 15·6. $C_{12}H_8N_2,C_{14}H_{14}N_2,2HCl$ requires Cl, 15·35%).

Phenazine–Base Complexes.—In each case, warm saturated solutions of the components, in various molecular ratios, were mixed in suitable solvents (light petroleum, ether, alcohol, acetone, benzene, or mixtures of these) and cooled or concentrated till the material crystallised, combined or otherwise. The following results were obtained:

(a) *Phenazine–*o*-phenylenediamine*, from alcohol, gave orange prisms, m. p. 153° (Found: C, 75·8; H, 5·4. $C_{12}H_8N_2,C_6H_8N_2$ requires C, 75·0; H, 5·55%).

(b) *Phenazine–*m*-phenylenediamine*, from alcohol, gave orange prisms, m. p. 143° (Found: C, 75·8; H, 5·6. $C_{12}H_8N_2,C_6H_8N_2$ requires C, 75·0; H, 5·55%).

(c) *Phenazine–*p*-phenylenediamine* crystallised in red prisms, m. p. 133°, from alcohol–light petroleum (Found: C, 73·4; H, 6·4. $C_{12}H_8N_2,2C_6H_8N_2$ requires C, 72·7; H, 6·1%).

(d) *Phenazine–diphenylamine* crystallised from alcohol in orange plates, m. p. 57—58° (Found: C, 83·7; H, 6·1. $C_{12}H_8N_2,2C_{12}H_{11}N$ requires C, 83·4; H, 5·8%).

1 : 2 : 3 : 4 : 9 : 10 : 11 : 12*-Octahydrophenazine.*—1 : 2 : 3 : 4-Tetrahydrophenazine (0·5 g.), sodium amalgam (15 g. of 4%), and alcohol (10 c.c.) were refluxed for 24 hours, the solution evaporated to crystallisation point, and the *product* recrystallised from alcohol, forming colourless plates (0·25 g.), m. p. 150°, an acid solution of which gave a deep purple coloration with ferric chloride (Found: C, 76·8; H, 8·75. $C_{12}H_{16}N_2$ requires C, 76·6; H, 8·5%).

2-*Methyl*-1 : 2 : 3 : 4-*tetrahydrophenazine*.—1-Methyl*cyclo*hexane-3 : 4-dione (Wallach, *Annalen*, 1918, **414**, 321; 1924, **437**, 182) (13 g.), *o*-phenylenediamine (11 g.), sodium acetate (15 g.), and glacial acetic acid (30 c.c.) were refluxed for 2 hours and poured into water and the solution was made alkaline and extracted with ether. The bulk of the product distilled at 144—148°/0·1 mm. (15 g.) and on redistillation at 147°/0·1 mm. gave a bright yellow *oil* (Found : C, 78·5; H, 6·9. $C_{13}H_{14}N_2$ requires C, 78·8; H, 7·1%).

2-*Methyl*-5 : 6 : 7 : 8-*tetrahydrophenazine*.—*p*-Methyl-*o*-phenylenediamine (3·6 g.), *cyclo*hexane-1 : 2-dione (3·3 g.), sodium acetate (5 g.), and glacial acetic acid (15 c.c.) were refluxed for 2 hours and the solution was poured into water, made alkaline, and extracted with ether. The *product* (5·5 g.) crystallised from light petroleum in yellow prisms, m. p. 78° (Found : C, 78·9; H, 7·5. $C_{13}H_{14}N_2$ requires C, 78·8; H, 7·1%).

2-*Methylphenazine*.—The above tetrahydro-compounds (2 g.) were separately refluxed with iodine (5·2 g.) in glacial acetic acid (10 c.c.) for 8 hours, the mixture cooled and made alkaline with dilute sodium hydroxide solution, and 2-methylphenazine distilled in superheated steam. It crystallised from light petroleum in light yellow needles (1 g.), m. p. 117° (Found : C, 80·6; H, 4·9. Calc. for $C_{13}H_{10}N_2$: C, 80·4; H, 5·15%).

Phenazine-2-*carboxylic Acid*.—2-Methylphenazine (1 g.), chromic acid (1·5 g.), and glacial acetic acid were refluxed for ½ hour, the product was poured into water and made alkaline, and the unchanged material extracted with ether; the aqueous solution was made acid, and the product extracted and crystallised from acetone, giving yellow needles (0·1 g.), m. p. 292° (Found : C, 69·7; H, 3·9. Calc. for $C_{13}H_8O_2N_2$: C, 69·7; H, 3·6%). The amide and its phenazhydrin were made by the method of Kögl and collaborators (*loc. cit.*).

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