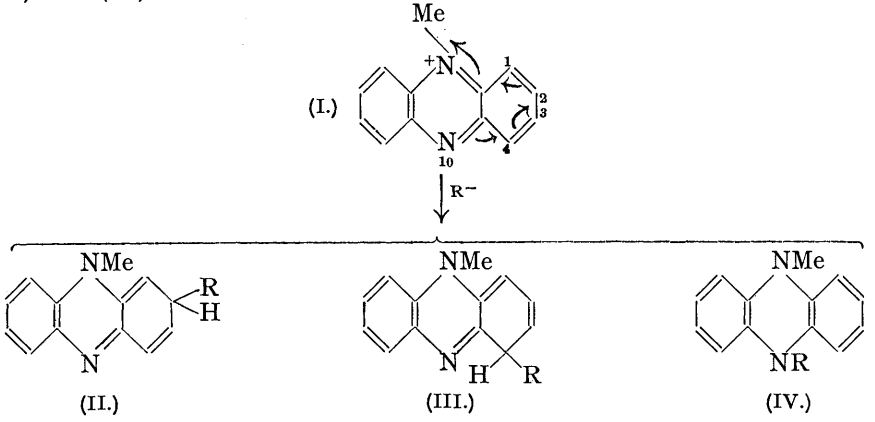
359. *The Phenazine Series. Part VI. Reactions of Alkyl Phenazonium Salts; the Phenazyls.*

By HENRY MCILWAIN.

The biological interest attached to pyocyanine (Friedheim, *Biochem. J.*, 1934, **28**, 173) and to *N*-methylphenazonium salts (Dickens, *ibid.*, 1936, **30**, 1064, 1233) suggested an investigation of the reactions of the latter compounds, and a number of keto-derivatives, sulphonic acids, and cyanides have been prepared by ionic attack of the phenazonium nucleus. Phenazonium salts differ markedly from compounds previously investigated (*e.g.*, quinolinium, acridinium salts) in the decomposition of the quaternary methohydroxide, and in the effect of visible radiation in the production of a keto-compound. Examples of free radicals in the phenazine series, which it is proposed to term *phenazyls*, have been discovered; they represent the bases of the semiquinonoid salts recently studied by Michaelis (*Chem. Reviews*, 1935, **16**, 243).

PREVIOUSLY recorded instances of nuclear attack of phenazonium, phenazoxonium, and phenazthionium salts have been confined to the action of oxidising agents, alone or in the presence of bases, which have invariably caused substitution in the 2-position. Under various conditions, facile substitution has now been observed in the 2-, 4-, and 10 (*N'*)-positions of phenazonium salts, which suggests that the molecule can be activated according to the mechanism indicated in (I) and that the primary products are the dihydro-derivatives (II), (III), and (IV):



Kehrmann (*Ber.*, 1913, **46**, 341) demonstrated that phenazine methosulphate reacted with ammonia in the presence of air with the production of 2-aminophenazine methosulphate, and suggested that with oxygen alone it yielded 2-keto-*N*-methylphenazine. This has now been proved by the isolation of the red product of oxidation and its comparison with the 2-keto-*N*-methylphenazine prepared by the later method of Kehrmann and Cherpillod (*Helv. Chim. Acta*, 1924, **7**, 973), though both specimens melted higher than is recorded by those authors. The yield varied with temperature, but was never greater than 5%, the bulk of the product being phenazine. Such oxidative demethylation has also been observed in naphthaphenazonium salts (Fischer, *Ber.*, 1893, **26**, 180) and in pyocyanine (Wrede and Strack, *Z. physiol. Chem.*, 1929, **181**, 68), and 2-hydroxyphenazine has now been obtained from 2-keto-*N*-methylphenazine under the conditions of the latter reaction.

N-Methylphenazonium hydroxide, presumably the immediate product of the reaction between *N*-methylphenazonium salts and alkalis, was found to be unstable even in the absence of air; in aqueous solution, a precipitate of phenazine and *N*-methyldihydrophenazine was formed, and formaldehyde detected. Quantitative experiments showed the reaction to follow the equation

$$2C_{13}H_{11}N_2{\cdot}OH \longrightarrow C_{13}H_{12}N_2 + C_{12}H_8N_2 + CH_2O + H_2O$$

which is closely analogous to the decomposition of methoxytrimethylammonium iodide observed by Dunstan and Goulding (J., 1899, **75**, 797)

$$OMe{\cdot}NMe_3I \longrightarrow NHMe_3I + CH_2O$$

and of methoxyphenyldimethylammonium iodide to dimethylaniline hydriodide and formaldehyde (Bamberger and Tschirner, *Ber.*, 1899, **32**, 1882). It is suggested that the complete decomposition of the phenazonium salt to dihydrophenazine and formaldehyde does not occur owing to part of the salt acting as hydrogen acceptor and forming equivalent amounts of phenazine and *N*-methyldihydrophenazine. This decomposition prevents the formation of pure methylphenazonium salts through the hydroxide (compare Browning, Cohen, and coll., *Proc. Roy. Soc.*, 1922, *B*, **93**, 329). The small amount of 2-keto-*N*-methylphenazine produced by alkaline oxidation of phenazonium salts is probably derived from the *N*-methyldihydrophenazine, which was observed to produce phenazine and a little 2-keto-*N*-methylphenazine on oxidation. Formaldehyde was also detected in the products of anaerobic alkaline decomposition of the two keto-*N*-methylphenazines.

Under the influence of visible light, oxidation of *N*-methylphenazonium salts occurred more rapidly and produced mainly the 4-keto-compound, pyocyanine, in much greater yield (45 mol. %), together with phenazine (47 mol. %) and small amounts of 1-hydroxyphenazine and 2-keto-*N*-methylphenazine. The reaction proceeded in this manner in acidic, neutral, or slightly alkaline aqueous solutions, but did not take place in alcohol or chloroform. It is probable that the 2-keto-*N*-methylphenazine produced in this reaction is formed by the normal dark reaction, and the 1-hydroxyphenazine by demethylation of pyocyanine. Photochemical reactions possibly analogous to that described above have been recorded in the production of quinhydrone from quinol (Hartley and Little, J., 1911, **99**, 1079) and in the isomerisation of tris-*p*-aminophenylacetonitrile (Liftschitz and Joffe, *Z. physikal. Chem.*, 1921, **97**, 426). The present synthesis of pyocyanine is much simpler than the original method of Wrede and Strack (*Z. physiol. Chem.*, 1928, **177**, 184; 1929, **181**, 58). As the introduction of a nuclear keto-group is a reaction which occurs biologically, the production of pyocyanine from *N*-methylphenazonium salts may constitute a biosynthesis. Light is not necessary for the pigmentation of *B. pyocyaneus*, but it was considered possible that the production of pyocyanine might be an enzyme reaction, and the action of tyrosinase on methylphenazonium salts was accordingly investigated; no action took place over the range of p_H within which the enzyme is active.

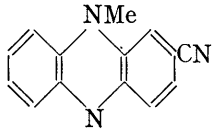
Phenazine ethosulphate, prepared by direct addition of ethyl sulphate at 150°, does not lose its alkyl group with the facility of the *N*-methyl compound, but is comparable with the *N*-phenyl derivatives in stability and, like those compounds, forms a 2-ketophenazine in excellent yield by oxidation in alkaline solution. Photochemical oxidation of the etho-

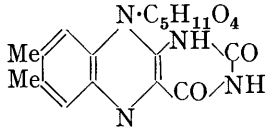
sulphate yields 4-keto-*N*-ethylphenazine; phenazine is not produced as a by-product, and neither of the keto-*N*-ethyl compounds undergoes ready dealkylation.

The reaction of phenazine methosulphate with sodium cyanide proceeded slowly in dilute aqueous solution and yielded mainly phenazine. In more concentrated solution, N-*methyldihydrophenazine-2-nitrile* was isolated in 60% yield. This was demethylated on heating with the production of a phenazine nitrile which yielded phenazine-2-carboxylic acid on hydrolysis; these reactions do not prove the relative positions of the Me and the CN group in the original compound, which are assumed from the mechanism of the reaction and from analogous instances to be as indicated in (II).

As a by-product in the preparation of *N*-methyldihydrophenazine-2-nitrile, a less soluble, dark blue compound was separated whose analysis indicated the formula $C_{14}H_{10}N_3$. This differs from that of the dihydrophenazine derivative in having one less hydrogen atom, and the by-product is converted into the dihydro-compound on reduction; the reverse reaction was performed by oxidation under a variety of conditions (air in markedly acid or alkaline solution; lead peroxide in ether; nitrous acid). The state of oxidation of the phenazine nucleus in the two compounds was also shown quantitatively by titration with iodine in acid solution, a process first applied to the phenazine series by Wohl (*Ber.*, 1903, **36**, 4135); the dihydro-compound required two equivalents of iodine in oxidation to the holoquinonoid salt, and the blue compound, whose acid solutions were of the green colour characteristic of semiquinones in the phenazine series (Michaelis, *loc. cit.*) required, like those compounds, one equivalent of iodine per phenazine nucleus.

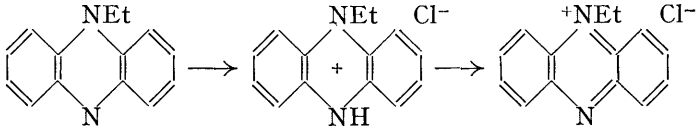
Unlike that of the phenazine–dihydrophenazine complexes which represent an intermediate stage in the oxidation of non-alkylated phenazine compounds, the colour of the blue nitrile, which closely resembles that of the simpler phenazhydrins, persists in its solutions (compare Clemo and McIlwain, J., 1934, 1991). The molecular size can therefore be determined by measurement of molecular weight, and such values, determined ebullioscopically in chloroform, definitely indicated the C_{14} formula. The compound must therefore possess an atom of unusual valency, probably, by analogy with the diphenyls of Wieland, the non-alkylated nitrogen atom, as is represented in (V), and the name N-*methylphenazyl-2-nitrile* is suggested. It would appear likely that one condition for the formation of stable free radicals in such compounds is the possession of a nitrogen substituent which, not having the mobility of a hydrogen atom, does not permit of the dismutation which takes place in the phenazhydrins on solution.

(V.) 



(VI.)

Qualitative evidence was obtained for the production of a phenazyl on oxidation of *N*-methyldihydrophenazine in non-aqueous solutions, which rapidly became red in air; but it was not possible to isolate the compound in a pure condition owing to its decomposition with formation of phenazine. The *N*-ethyl compound was, however, stabler in this respect, and a dark purple N-*ethylphenazyl* was prepared by oxidation of N-*ethyldihydrophenazine* (obtained by reduction of *phenazine ethosulphate*) in ethereal or in benzene solution. It possessed the iodine equivalent and molecular weight corresponding to $C_{14}H_{13}N_2$. The conversion of a phenazyl into a semiquinonoid salt (using Michaelis's representation of these compounds) and its subsequent oxidation can then be formulated:



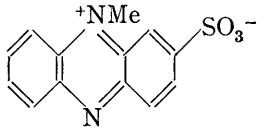
(VII.) (VIII.) (IX.)

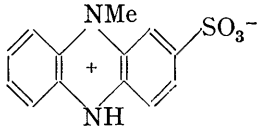
though Michaelis could regard bases of the type (VII) as hypothetical only (*J. Amer. Chem. Soc.*, 1933, **55**, 1482). The phenazyls are comparable with the partly reduced lactoflavine

(VI), established recently by Kuhn and Ströbele as a free radical (*Ber.*, 1937, **70**, 753). Compounds described as nitrodihydrophenazines by Kehrmann and Messinger (*Ber.*, 1893, **26**, 2374) and by Leemann and Grandmougin (*Ber.*, 1908, **41**, 1309) possess properties unusual in dihydrophenazines but closely similar to those of the phenazyls here described, and the analytical figures of those authors are invariably in better agreement with the corresponding phenazyl.

The reaction of phenazine methosulphate with sodium sulphite produced a little *N*-methyldihydrophenazine, and a mixture of mono- and di-sulphonic acid, the former of which was separated by the lesser solubility of its sodium salt in water. This *sodium* N-*methyldihydrophenazinesulphonate* is assumed to be the 2-compound by analogy with the preceding reactions; it has not been found possible to obtain a derivative of known configuration from it. Heating with potassium hydroxide and cyanide in an attempt to obtain such a compound yielded only phenazine; demethylation was readily brought about by heat.

Sodium *N*-methyldihydrophenazinesulphonate is readily oxidised in solution, and the process was followed quantitatively by iodine titration. Complete oxidation with two equivalents yielded an *N*-methylphenazonium salt (X), crystallising from water in yellow needles; partial oxidation afforded a deep green compound, $C_{13}H_{11}O_3N_2S$, which possessed

(X.) 



(XI.)

the properties of the internal semiquinonoid salt (XI) of *N*-methylphenazyl-2-sulphonic acid. The holoquinonoid sulphonic acid was susceptible to further substitution; sodium sulphite formed a labile dihydro-disulphonic acid; this was isolated as its semiquinonoid salt, and underwent quantitative oxidation to the holoquinonoid compound. Qualitative evidence was also obtained for attack by hydroxyl and cyanide ions. The dihydro-disulphonic acid is identical with the compound isolated from the initial reaction between phenazine methosulphate and sodium sulphite, which proceeds to completion only in the presence of excess of sulphite; both mono- and di-sulphonic acid are also formed during the reduction of the methosulphate with hyposulphite. The biological properties of these sulphonic acids, and of the keto-*N*-ethylphenazines, will be described elsewhere. Qualitative evidence has been obtained for the production of thiophenazones by the action of sodium sulphide on phenazine methosulphate and ethosulphate.

Substitution in the *N'*-position of the phenazonium nucleus was observed in the action of methylmagnesium iodide on phenazine methosulphate, which yielded *NN'*-dimethyldihydrophenazine; this affords a much more convenient method of preparation of this compound, which has been shown to possess biological action (Dickens, *Biochem. J.*, 1936, **30**, 1064), than was formerly available (Clemo and McIlwain, J., 1935, 738).

Experimental.

Oxidation of Phenazine Methosulphate.—The salt (2·0 g.) and sodium carbonate (0·3 g.) in water (50 c.c.) at room temperature were exposed to the air for 1 week; red crystals, consisting largely of phenazine, were deposited. The whole was evaporated to dryness, the residue extracted with the minimum amount of alcohol, twice the volume of water added, and the alcohol removed, leaving a precipitate of phenazine (1·0 g.), and in solution 2-keto-*N*-methylphenazine, which, recrystallised from water, formed deep red prisms (0·05 g., m. p. 200°; compare Kehrmann and Cherpillod, *loc. cit.*). Preliminary experiments were performed in which the yield of 2-keto-*N*-methylphenazine was estimated by colorimetric comparison with a solution of the product containing 1 mg./10 c.c.; these indicated that the yield was not increased by the addition of oxidising agents, and was appreciably decreased by carrying out the reaction at higher temperatures.

Oxidation of N-*Methyldihydrophenazine.*—The compound (1·0 g.) in alcohol (50 c.c.) was exposed to the air for 4 days; the solution became rich red, and after concentration was separated as described above into phenazine (0·8 g.) and 2-keto-*N*-methylphenazine (0·05 g.). Oxidation

with lead peroxide and with silver oxide afforded similar results. It was, however, observed that the first product of oxidation was blue-red, was extracted from its aqueous alcoholic solution by ether, and formed a green salt with acids; it is presumably *N*-methylphenazyl, and the above air oxidation, as in the case of the 2-nitrile, was accelerated by the presence of potassium hydroxide in the alcoholic solution.

Demethylation of 2-*Keto*-N-*methylphenazine.*—The keto-compound (0·1 g.) in sodium hydroxide solution (50 c.c. of 2%) with hydrogen peroxide (1 c.c. of 20 vol.), heated at 80° for 1 hour, lost its bright red and became a browner colour; while the solution was warm, acetic acid was added in excess, and after standing, the fine red precipitate of hydrated 2-hydroxyphenazine (0·06 g.) was collected; m. p. 254°, undepressed by a specimen prepared by Kehrmann's method.

Reaction of Phenazine Methosulphate with Alkali.—To the salt (0·100 g.; 0·000327 mol.) in water (20 c.c.) in a distilling flask through which a slow stream of oxygen-free nitrogen was passed, 10% sodium carbonate solution (10 c.c.) was added, and two-thirds of the liquid distilled into a little ice-cooled water. Decomposition took place on warming and some phenazine steam-distilled; more water was added to the flask, and the distillation repeated. The distillate was filtered, and formaldehyde estimated by the method of Bodea (*Bull. Soc. chim.*, 1930, **47**, 1408): 5 : 5-dimethyldihydroresorcinol solution (2 c.c. of 10% alcoholic) was added, the whole heated at 100° for 10 minutes, and kept for 2 hours. The precipitate was dried at 100° and weighed (0·045, 0·047 g., equiv. to 0·000154, 0·000162 mol.; m. p. 186°, undepressed by admixture with genuine formaldehyde-dimedon). Control experiments showed that 98% of a known amount of formaldehyde could be removed from aqueous solution and estimated in this way.

The residue in the distilling flask dissolved in dilute acid to a green solution, which was titrated immediately with N/50-iodine solution until the phenazine compounds had been oxidised to their yellow holoquinonoid salts (16·3, 16·0 c.c.; 0·000326, 0·000320 mol.). Starch was used as external indicator, and the end-point could also be judged by the appearance of an opalescence due to excess of iodine forming insoluble periodides. The presence of methylphenazonium salts in the oxidised solution was established in a reaction performed on a larger scale by the isolation of the slightly soluble iodide (m. p. 169°). Similar quantitative results were obtained in the reaction between phenazonium salts and sodium acetate; but the amount of formaldehyde isolated when the decomposition was affected by means of sodium hydroxide was smaller, presumably owing to its polymerisation by the alkali.

Pyocyanine was decomposed by sodium carbonate, and 2-keto-*N*-methylphenazine by sodium hydroxide, again with the production of formaldehyde and reduced compounds, but the reactions did not proceed quantitatively.

Photochemical Oxidation of Phenazine Methosulphate.—The salt (2·0 g.) in water (2 l.) was exposed to sunlight in an open flask until no further change took place, as was judged by colorimetric comparisons of portions of the reacting solution, made alkaline by addition of sodium carbonate, with a standard solution of pyocyanine (1 mg./10 c.c.). This occurred after about 50% of the theoretical amount of pyocyanine had been formed, and in the course of about 1 day. 10% Sodium carbonate solution (40 c.c.) was added, the whole fully extracted with chloroform, and the extract dried with potassium carbonate and evaporated under reduced pressure to 20 c.c. Hot light petroleum was added, the solution allowed to cool, and the deep blue crystalline precipitate of pyocyanine (0·65 g.) collected and recrystallised from water. It was identified by its m. p. (133°) and by degradation (Wrede and Strack, *Z. physiol. Chem.*, 1928, **177**, 177) to 1-hydroxyphenazine (m. p. 154°, undepressed by admixture with an authentic specimen).

The petroleum mother-liquors were fully extracted with water, the extract concentrated to crystallisation under reduced pressure, and the product recrystallised from water, yielding red prisms, identified by m. p. and mixed m. p. (200°) as 2-keto-*N*-methylphenazine (0·05 g.). The washed petroleum solution was further extracted with dilute aqueous alkali, the extract acidified with acetic acid, and the yellow precipitate obtained dried and crystallised from alcohol, giving 1-hydroxyphenazine (0·05 g., m. p. 154°). The petroleum solution on evaporation to crystallisation now yielded phenazine (0·55 g., m. p. 171°).

When solutions of the phenazonium salt were exposed to light with the addition of oxidising agents (potassium ferricyanide or persulphate), these were reduced but the yield of pyocyanine was not altered.

Attempted Photochemical Oxidations.—Kehrmann's preparation of aminophenazine methosulphate (*loc. cit.*) could not be performed photochemically, as the reaction proceeded rapidly in concentrated solutions, and in dilute solutions it followed a different course, apparently

yielding *N*-methylphenazyl; phenazine was the only product isolated. The oxidation of pyridinium (" Organic Syntheses," **1935**, **15**, 41), quinolinium (J., **1913**, 1977), and acridinium salts (*J. pr. Chem.*, **1892**, **45**, 193) did not proceed differently in sunlight.

Reaction of Phenazine Methosulphate with Cyanide.—Sodium cyanide (1·0 g.) in water (5 c.c.) was added gradually with shaking to a cooled suspension of finely powdered phenazine methosulphate (4·0 g.) in chloroform (15 c.c.). After ¼ hour, the aqueous layer had become colourless and contained sodium methyl sulphate; blue crystals had formed in the chloroform layer and were filtered off, washed with chloroform, and recrystallised from that solvent, forming blue needles (0·35 g.), m. p. 145°, of N-*methylphenazyl-2-nitrile* (Found: C, 76·1; H, 4·5; iodine equiv., 224, 228; *M*, in chloroform, 227, 217. $C_{14}H_{10}N_3$ requires C, 76·4; H, 4·5%; iodine equiv. and *M*, 220). The compound forms blue-green solutions in organic solvents, and dissolves in dilute mineral acids to the emerald-green semiquinone, becoming colourless with zinc and yellow with persulphate.

The chloroform mother-liquors were combined, the solvent removed, the brown residue extracted repeatedly with hot benzene, and the solution concentrated, yielding bright yellow needles of N-*methyldihydrophenazine-2-nitrile* (1·7 g.). From the cooler solvent this compound separated in stout yellow-green prisms; both forms on drying at 100° fell to a yellow powder m. p. 155° (Found: C, 75·7; H, 4·8; iodine equiv., 113, 115. $C_{14}H_{11}N_3$ requires C, 76·0; H, 4·8%; iodine equiv., 110·5). The compound is soluble in dilute acids to yellow solutions, becoming first green and then bright yellow on oxidation.

The material not extracted by benzene could not be obtained in crystalline condition, but on sublimation under reduced pressure at 240° for 10 hours, phenazine (0·2 g.) and a little phenazine-2-nitrile were obtained. When the initial reaction was performed in more dilute aqueous solution, a much greater quantity of phenazine was produced.

Interconversion of the N-*Methyl Nitriles.*—(*a*) The dihydro-base (0·1 g.) in alcohol (10 c.c.) containing potassium hydroxide (0·2 g.) remained unchanged in an atmosphere of nitrogen, but in air darkened in colour, and blue crystals of *N*-methylphenazyl-2-nitrile separated (0·08 g., m. p. 145°).

(*b*) The dihydro-base (0·1 g.) in 10% hydrochloric acid (5 c.c.) dissolved to a yellow solution, which became deep green on standing in air for 1 hour; excess of sodium hydroxide produced a blue sludge, which was extracted with chloroform, the extract, dried (potassium carbonate) and concentrated to crystallisation, giving *N*-methylphenazyl-2-nitrile (0·07 g.).

(*c*) To the dihydro-base (0·1 g.) in alcohol (10 c.c.) were added sodium nitrite (0·05 g.) in water (2 c.c.), and sulphuric acid (2%) drop by drop with shaking, with the intention of preparing a nitroso-derivative. The phenazyl (0·08 g.) separated.

(*d*) *N*-Methylphenazyl-2-nitrile (0·1 g.) in alcohol, sodium hydroxide (0·2 g.) in water (2 c.c.), and sodium hyposulphite (0·2 g.) in water (2 c.c.) were mixed in an atmosphere of nitrogen in a tap-funnel; the solution rapidly became yellow. An equal volume of chloroform was added, the aqueous layer separated, and the chloroform washed with water. When free from alkali it was no longer sensitive to air, and was dried (sodium sulphate), the solvent removed, and the residue crystallised from benzene, yielding *N*-methyldihydrophenazine-2-nitrile (0·07 g.).

Phenazine-2-carboxylic Acid.—Both of the *N*-methyl nitriles changed above 80° and a higher-melting compound slowly sublimed. Either compound (0·1 g.), heated in a loosely corked tube at 200° for 12 hours, gave a yellow sublimate (0·03 g.), crystallising from alcohol in fine sulphur-yellow needles, m. p. 226°. This compound (0·1 g.) in alcohol (10 c.c.) containing potassium hydroxide (1 g.) was refluxed for 2 hours; ammonia was evolved. An equal volume of water was added, the alcohol removed, the solution acidified, and the flocculent precipitate collected, dried, and crystallised from acetone, yielding yellow needles of phenazine-2-carboxylic acid (0·07 g.), m. p. 284°, not depressed by admixture with an authentic specimen.

Attempted demethylation of the original nitriles in better yield by refluxing in xylene, or under the alkaline peroxide conditions used for the keto-compounds, was not successful; the latter reaction produced a little phenazine-2-carboxylic acid.

Sodium N-*Methyldihydrophenazinesulphonate.*—Phenazine methosulphate (5 g.) in water (30 c.c.) and sodium sulphite (2·5 g.) in water (15 c.c.) were mixed with cooling; the yellow solution darkened to brown-red and became opalescent in the course of 1 minute; it was warmed slightly and kept for ¼ hour; a bulky grey crystalline precipitate then separated. This was filtered off with minimum exposure to the air, washed free from inorganic matter with water and from *N*-methyldihydrophenazine with alcohol, followed by chloroform, recrystallised from water containing a little reducing agent ($NaHSO_2$), and dried in a vacuum at 20°, giving the hydrated *sodium* salt in colourless plates (1·7 g.) (Found: C, 49·0; H, 4·1; iodine equiv., 162.

$C_{13}H_{11}O_3N_2SNa,H_2O$ requires C, 49·3; H, 4·1%; iodine equiv., 158). On drying at a higher temperature, decomposition took place and the analytical figures approximated to those of the demethylated compound; on standing in air, the compound and its solutions became red.

From the chloroform portion of the washings, *N*-methyldihydrophenazine (0·6 g.) was isolated. The aqueous layer was evaporated under reduced pressure of nitrogen to 10 c.c.; sodium *N*-methyldihydrophenazinesulphonate (0·55 g.) then separated. The mother-liquors from this crystallisation had an intense greenish fluorescence due to the disulphonic acid, which was isolated as its internal semiquinonoid salt (1·85 g.) (see below).

N-*Methylphenazylsulphonic Acid Betaine.*—To a solution of sodium *N*-methyldihydrophenazinesulphonate (1·0 g.) in 10% sulphuric acid (10 c.c.), potassium persulphate (0·5 g. in the minimum quantity of water) was added; a green crystalline precipitate gradually formed. The solution was kept for 2 hours, and the *product* was then collected, recrystallised from water, and dried in a vacuum at 80° (0·7 g., not melting at 300°) (Found: C, 56·3; H, 4·2; iodine equiv., 276. $C_{13}H_{11}O_3N_2S$ requires C, 56·7; H, 4·0%; iodine equiv., 275).

N-*Methylphenazoniumsulphonic Acid Betaine.*—To the phenazylsulphonic acid (1·0 g.) in 10% sulphuric acid (10 c.c.), a saturated solution of potassium persulphate was added until the whole became a golden-yellow solution; this was concentrated to crystallisation, yielding yellow needles (0·8 g.) (Found: C, 56·75; H, 3·8. $C_{13}H_{10}O_3N_2S$ requires C, 56·9; H, 3·65%).

Sodium Hydrogen N-*Methylphenazyldisulphonate Betaine.*—To a solution of the above holoquinonoid salt (1·0 g.) in water (20 c.c.), sodium sulphite (0·5 g.) in water (5 c.c.) was added; the solution became orange-red with a green fluorescence, and an impure specimen of sodium *N*-methyldihydrophenazinedisulphonate was obtained by precipitation with alcohol and crystallisation from aqueous alcohol (Found: iodine equiv., 210. Calc. for $C_{13}H_{10}O_6N_2S_2Na_2$: iodine equiv., 200). The whole was converted into the readily crystallised semiquinone by the addition of 20% sulphuric acid (2 c.c.) and potassium persulphate (0·4 g.); deep green needles separated, and were recrystallised from water and dried in a vacuum at 100° (1·0 g.) (Found: C, 41·5; H, 2·7; iodine equiv., 385, 380. $C_{13}H_{10}O_6N_2S_2Na$ requires C, 41·4; H, 2·7%; iodine equiv., 377).

Phenazine Ethosulphate.—Phenazine (5·0 g.) and ethyl sulphate (7 c.c.) were heated at 150° until a test portion dissolved completely in water (40 minutes); the mixture was then cooled, and crystallised from alcohol, yielding the *salt* in brown prisms (8·5 g.), m. p. 190° (Found: C, 57·55; H, 5·6. $C_{12}H_8N_2,Et_2SO_4$ requires C, 57·4; H, 5·4%).

2-*Keto*-N-*ethylphenazine.*—To a solution of phenazine ethosulphate (1·0 g.) and potassium ferricyanide (2·0 g.) in water (40 c.c.), 10% sodium hydroxide solution (5 c.c.) was added gradually, with stirring. The mixture became dark red and the *keto*-compound separated as an oil which became solid on rubbing; it crystallised from water or benzene in dark red needles (0·6 g.), m. p. 174° (Found: C, 57·1; H, 5·3. $C_{14}H_{12}ON_2$ requires C, 75·0; H, 5·35%). The compound formed yellow salts with mineral acids, which were hydrolysed to the red salts of the keto-compound; it was less soluble in water and in benzene than 2-keto-*N*-methylphenazine. By substituting ethyl sulphate for methyl sulphate in Kehrmann's preparation of 2-keto-*N*-methylphenazine (*loc. cit.*) a compound was produced identical with that described above.

4-*Keto*-N-*ethylphenazine.*—Phenazine ethosulphate (1·0 g.) and sodium carbonate (0·16 g.) in water (1 l.) were kept in daylight with occasional shaking until colorimetric comparison showed no further production of the blue keto-compound (about 10 hours in sunlight; 4 days in diffuse light). Further sodium carbonate solution was added (40 c.c. of 10%), the whole extracted with chloroform, the extract dried (potassium carbonate), and the solvent removed; the residue crystallised from benzene in dark blue needles (0·55 g.), m. p. 187° (Found: C, 75·2; H, 5·3. $C_{14}H_{12}ON_2$ requires C, 75·0; H, 5·35%). The *compound* is less soluble in water and in benzene than is pyocyanine.

N-*Ethyldihydrophenazine.*—Phenazine ethosulphate (5 g.) in water (100 c.c.) and zinc dust (5 g.) were placed in a tap-funnel in an atmosphere of nitrogen, 20% sulphuric acid (20 c.c.) and ether (50 c.c.) added, and the whole, agitated by the gas stream, kept until the aqueous layer became colourless; it was then run off, and the ethereal solution of the *dihydro*-compound dried and evaporated under reduced pressure of nitrogen at room temperature. The residue (2·5 g.), recrystallised from benzene with minimal exposure to air, formed colourless prisms, m. p. (in nitrogen) 99° (Found: C, 80·2; H, 6·5. $C_{14}H_{14}N_2$ requires C, 80·0; H, 6·7%).

N-*Ethylphenazyl.*—*N*-Ethyldihydrophenazine (3·0 g.) in dry ether (120 c.c.) was shaken with dry lead peroxide (3 g.) and sodium sulphate (6 g.) for 10 hours. The rich red solution was filtered, concentrated, and cooled in ice–salt. An intensely red, crystalline precipitate formed, and was recrystallised from ether in the same manner, yielding the pure *phenazyl* (0·7 g.), m. p.

102° (Found : C, 80·7; H, 6·2; iodine equiv., 212, 214; *M*, in chloroform, 206, 219. $C_{14}H_{13}N_2$ requires C, 80·4; H, 6·2%; iodine equiv. and *M*, 209).

NN′-*Dimethyldihydrophenazine.*—To finely powdered phenazine methosulphate (1·0 g.) in ether (50 c.c.), stirred in a nitrogen atmosphere and cooled in ice, methylmagnesium iodide (from magnesium, 0·15 g.; methyl iodide, 0·4 c.c.) was added gradually. The mixture was refluxed for ½ hour and then washed with water; the yellow aqueous layer contained unchanged quaternary salt, recovered as the iodide (0·4 g.). The ethereal solution contained *N*-methyl-*NN′*-dihydrophenazine and *N*-methyldihydrophenazine. The latter (0·1 g.) was removed by washing with 5% sulphuric acid; the former (0·25 g.), obtained by removal of the ether, crystallised from benzene in colourless prisms, m. p. 152°, undepressed by the specimen previously prepared (Clemo and McIlwain, *loc. cit.*).

I wish to acknowledge my indebtedness to Professor R. Robinson for advice received in connection with this work, to Professor H. S. Raper for a preparation of tyrosinase, and to the Department of Scientific and Industrial Research for a research award.

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