SYNTHESIS OF SOME PHENAZINE DERIVATIVES[1]

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ABSTRACT

Nitration of 2-amino-, 2-N-methylamino-, and 1-amino-phenazine resulted in the formation of 2-amino-1-nitro-, 2-N-methylamino-1-nitro-, and 1-amino-4-nitro-phenazine, respectively. Nitration of 2-aminophenazine was shown to proceed via the intermediate nitramine, which was isolated and identified. 2-Hydroxy-1-nitrophenazine was found to exist in the solid state exclusively in the hydroxy form, and 4-nitro-1(5H)-phenazinone was the only solid obtained on acidification of a 1-hydroxy-4-nitrophenazine salt solution.

DISCUSSION

In a continuation of the studies dealing with the structure and reactivity of aza-aromatic nitramines (1–3), an investigation of the behavior of phenazine nitramine derivatives was undertaken.

2-Aminophenazine (I) (4) was nitrated in concentrated sulphuric acid with 70% nitric acid at temperatures between −50° and −15°. This resulted in the formation of 2-nitraminophenazine, in an almost quantitative yield. The nitramine obtained in this way was found to be a mixture of the monohydrate (II) and anhydrous (III) forms, the former being the main component. On prolonged drying, II was gradually transformed into the anhydrous form (III). The pure monohydrate was prepared by slow crystallization from a dilute acidic solution of the mixture. When dried by benzene distillation at 50°, both the monohydrate and the mixture of the two forms yielded the anhydrous nitramine.

Both the monohydrate and the anhydrous nitramine decomposed rapidly when heated to 150–160°. No differences in the chemical behavior of the two forms were observed. They were weakly acidic, dissolved in dilute alkali, and could be reprecipitated from solution with dilute acids. When treated with concentrated sulphuric acid, the nitramines (II, III) were rearranged to 2-amino-1-nitrophenazine (IV).

The infrared spectra of the two forms were in agreement with the proposed structures. In the spectrum of the monohydrate (II), the broad band with maxima at 3540, 3400, and 3200 cm^{-1} indicated the presence of water of crystallization. Absorption which could be attributed to $\overset{+}{N}$—H stretching and to —NO_2 symmetrical vibrations were present in the spectra of the two forms, and the absorption patterns in the range 900–700 cm^{-1} were in agreement with a phenazine substituted in position 2. Distinguishing features between the spectra of II and III were the presence of peaks at 855 and 790 cm^{-1} in the spectrum of III which did not appear in that of II and the difference in the frequency and shape of the bands assigned to the $\overset{+}{N}$—H stretching vibrations (a broad weak band at 2700 cm^{-1} in the spectrum of II and a broad unresolved band between 3100 and 2700 cm^{-1} in that of III). The presence of an $\overset{+}{N}$—H absorption in the spectra of both forms and the

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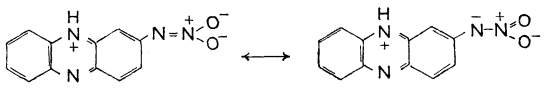
FORMULAE SHEET



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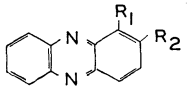
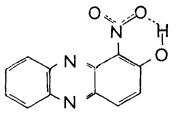
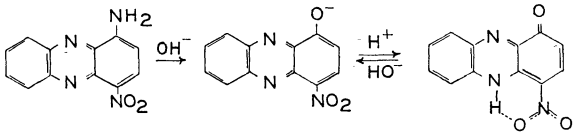


I: $R_1=H$; $R_2=NH_2$
IV: $R_1=NO_2$; $R_2=NH_2$
V: $R_1=R_2=NH_2$
VIII: $R_1=H$; $R_2=NH-CH_3$
IX: $R_1=H$; $R_2=N(CH_3)(COCH_3)$
X: $R_1=NO_2$; $R_2=NHCH_3$
XI: $R_1=NH_2$; $R_2=H$



VI



XIV XVI XVII

shift of the $-NO_2$ symmetric vibrations to higher frequencies suggested a nitriminophenazinium inner-salt structure for the nitramines (II, III). Such a structure had been proposed previously (5) for other aza-aromatic nitramines.

Rearrangement of 2-nitraminophenazine was carried out in concentrated sulphuric acid at 0°. After 3 hours, isomerization was complete and 2-amino-1-nitrophenazine (IV), the main rearrangement product, was obtained in a 55% yield. The aminonitro compound (IV) was basic, and dissolved readily in 5% hydrochloric or sulphuric acid. Direct nitration of 2-aminophenazine (I) performed under conditions similar to those of rearrangement resulted in the formation of IV in a slightly lower yield. Thus it would appear that in direct nitration, formation of IV occurred via rearrangement of the intermediate nitramine.

Proof for the structure of the aminonitro derivative (IV) was obtained in several ways. When IV was oxidized in an alkaline medium with potassium permanganate, the production of quinoxaline-2,3-dicarboxylic acid showed that only one carbocyclic ring in IV was substituted. Reduction of IV provided a diamine, of necessity 1,2-diaminophenazine (V). The aminonitro compound IV on being refluxed with concentrated hydrochloric acid or boiled with 1% aqueous sodium hydroxide was converted into 2-hydroxy-1-nitrophenazine (VI) (6, 7). In the infrared spectrum of IV there were bands at 3430, 3290, and 3170 cm^{-1} in the N—H stretching region, and peaks at 1520 and 1280 cm^{-1} which could be correlated with the asymmetric and symmetric vibrations of the nitro group. The lack of any bands between 900 and 850 cm^{-1} and the presence of a peak at 802 cm^{-1} were consistent with 1,2-substitution.

1,2-Diaminophenazine (V) was prepared both by zinc – acetic acid reduction and by

catalytic reduction of 2-amino-1-nitrophenazine (IV). When a methanolic solution of IV was reduced with hydrogen in the presence of a platinum catalyst, the color of the liquid changed from brown, to deep red, to colorless. On exposure to air, the colorless liquid became deep red again, and a product, identical with the diamine (V) obtained by zinc – acetic acid reduction, was isolated. The colorless methanolic solution was considered to contain a product of further reduction, most probably 1,2-diamino-5,10-dihydrophenazine (VII).

Hydrolytic replacement of the amino group of 2-amino-1-nitrophenazine (IV) in acidic medium was very slow. On the other hand, the replacement reaction in alkaline medium proceeded in a straightforward fashion. It was complete within $1\frac{1}{2}$ hours, and a nearly quantitative yield of 2-hydroxy-1-nitrophenazine was obtained.

When *o*-nitroaniline and methylaniline hydrochloride were allowed to react in the presence of fused zinc chloride according to a modified Wohl–Lange procedure (4), a mixture consisting of approximately 15% 2-aminophenazine (1) and 85% 2-N-methylaminophenazine (VIII) was obtained. Separation of the amines was achieved by chromatography. Acetylation of VIII provided 2-N-acetyl-N-methylaminophenazine (IX). Nitration of the N-methylamine (VIII) in concentrated sulphuric acid with nitric acid (70% excess) at temperatures below −20° resulted in the immediate formation of 2-N-methylamino-1-nitrophenazine (X).

It has been established (8–11) that nitration of electron-deficient aza-aromatic amines proceeded mainly by an "indirect route", and that in cases in which the intermediate nitramine was not formed, the amine resisted nitration. Since the nitration of the N-methylamine (VIII) took place under such mild conditions, it was believed that 2-methylamino-1-nitrophenazine (X) was produced by the intramolecular rearrangement of an unstable intermediate nitramine. Had a direct nitration occurred, much more vigorous reaction conditions would have been necessary and different products would likely have been formed. The nitration of 2-aminophenazine (I) had been considered to proceed by the same reaction mechanism. In the case of the N-methylamine (VIII), however, nitration occurred at a much faster rate, and the reaction resulted in a higher yield of product, 65% versus 55%, being obtained. The increased rate of rearrangement was expected since 2-nitraminophenazine (II, III) had already rearranged readily, and because it had been demonstrated in the pyridine series that introduction of a methyl group into the amino function decreased the stability of the intermediate nitramine in the rearrangement reaction. The fact that the nitro groups in both instances, migrated to position 1 of the phenazine nucleus provided additional support for the assumption that the same mechanism was operative in each case.

The structure proposed for the methylaminonitro compound (X) was substantiated by the infrared spectrum, which had bands indicating the presence of an N—H group, a methyl group, a nitro group, and 1,2-substitution. Further evidence for the structure of X was obtained by its transformation to 2-hydroxy-1-nitrophenazine (VI) on treatment with a 1% sodium hydroxide solution.

1-Aminophenazine (XI) was prepared at first by the deamination of 1,3-diaminophenazine (XII) (12). The difficulties encountered in the deamination led to an investigation of alternative procedures for the synthesis of the amine. 1-Aminophenazine (XI) was reported (13) to have been obtained in a 50% yield by refluxing 2,2′-diaminodiphenylamine (XIII) with nitrobenzene. However, no details of procedure were given in the report and attempts to duplicate the published results failed. After considerable effort had been directed toward determining the exact reaction conditions for the oxidation,

it was found that by heating the diamine (XIII) with nitrobenzene in a nitrogen atmosphere, and removing the water formed in the reaction by distillation, 1-aminophenazine (XI) was obtained in a 40% yield.

The main mononitration product of 1-aminophenazine in concentrated sulphuric acid was found to be 1-amino-4-nitrophenazine (XIV). Nitration with a 30% excess of nitric acid for 1 hour was complete, but a considerable amount of a substance soluble in ammonia was produced simultaneously with XIV. The former was assumed to be 1-nitramino-4-nitrophenazine on the basis of its solubility in ammonia, rapid decomposition at the melting temperature, relative stability with respect to dilute acids, and the infrared spectrum of the crude product. Complete nitration of 1-aminophenazine with no detectable formation of polynitro compounds soluble in ammonia was achieved when a 70% excess of nitric acid was used and the reaction was terminated after 2 minutes. The structure of the aminonitro compound XIV was demonstrated by oxidation and reduction reactions, by its infrared spectrum, and by replacement of the amino group with an hydroxyl function.

Oxidation of 1-amino-4-nitrophenazine (XIV) in alkaline medium with potassium permanganate provided quinoxaline-2,3-dicarboxylic acid. Reduction of a methanolic solution of the aminonitro compound (XIV) with hydrogen and using a platinum catalyst resulted in a change in the color of the solution from brown to blue to colorless. The colorless solution, on exposure to air, became blue then changed to brown, and a brown solid precipitated. It was assumed that the final reduction product, which gave the colorless solution, was 1,4-diamino-5,10-dihydrophenazine. The colorless solution was rapidly oxidized by air back to the blue solution containing 1,4-diaminophenazine (XV). This sequence of reactions excluded the possibility of 1,2-substitution for the amino nitrophenazine (XIV), since 1,2-diaminophenazine (V) had been identified previously, and of 1,3-substitution because a methanolic solution of 1,3-diaminophenazine (XII) was red. The behavior of the aminonitro compound (XIV) on reduction with zinc – acetic acid provided further confirmation of 1,4-substitution, insofar as the solution of the reduction product in acetic acid was violet while the solutions of the 1,2-diamine (V) and the 1,3-diamine (XII) were brown and green respectively. The 1,4-diaminophenazine (XV) was isolated from the acetic acid solution in the form of blue needles when the acidic solution was rendered alkaline with ammonia in a nitrogen atmosphere. The substance did not melt below 300°, and in solution on exposure to air formed a brown unidentified product.

Additional evidence in favor of the proposed structure was accumulated when, on boiling of 1-amino-4-nitrophenazine (XIV) with aqueous alkali, 1-hydroxy-4-nitrophenazine (XVI), as its alkali salt, was produced. By acidifying the aqueous solution of the alkali salt (XVI), 4-nitro-1(5H)-phenazinone (XVII) was obtained. The alkaline solution of 2-hydroxy-1-nitrophenazine (VI), when acidified, gave the phenazinol tautomer exclusively.

The formation of XVII as the only solid tautomer, and the sole existence of the hydroxy tautomer of 2-hydroxy-1-nitrophenazine (VI) in the solid state, were explained by a hydrogen-bonding effect and formation of a stable six-membered chelate ring. The stability of the hydroxy tautomer in VI required the nitro group to be located in position 1, likewise in the case of XVII the nitro group must be in position 4.

Confirmatory evidence for the structure proposed for the phenazinone (XVII) was based on the reversible transformation of the compound into the ammonium salt of 1-hydroxy-4-nitrophenazine (XVI), the infrared spectra of XVI and XVII, and the

ultraviolet spectrum of XVII in aqueous solution. The general absorption pattern in the 900–700 cm^{-1} region of the infrared spectrum of XVI was similar to that of 1-amino-4-nitrophenazine (XIV) and constituted a clear indication of analogous structures. The absorption pattern in the same region for the phenazinone (XVII), however, was completely different, the two very characteristic bands at 820 ± 10 and 750 ± 15 cm^{-1}, which appeared in all the other phenazines studied, being absent.

4-Nitro-1(5H)-phenazinone (XVII) was soluble in water at 25° to the extent of 0.5 mg/ml. The red solution, on 10-fold dilution, became yellow in color. When this yellow solution was evaporated, red crystals of XVII were recovered. In acidic medium (pH 2.0) the phenazinone (XVII) was much less soluble, and the solution was red. These observations could be explained by an equilibrium in water solution between the phenazinone (XVII) and the hydroxy tautomer in its anionic form (XVI), the phenazinone being red and the anion yellow in color. This equilibrium was studied by means of ultraviolet spectroscopy. The aqueous solution of phenazinone (XVII) (4.15×10^{-5} mole/liter) absorbed at 425 mμ with a molar extinction coefficient of 13,970; no absorption occurred at wavelengths above 530 mμ. An alkaline solution of XVII of an equivalent concentration gave the same absorption curve, and it was concluded that at the given concentration, the phenazinone was already fully converted to the anion. An acidic solution of XVII (2 drops of 3.7% hydrochloric acid per 4 ml of solution) of the same concentration displayed a maximum at 400 mμ and a molar extinction coefficient of 12,050. It also absorbed markedly at 530 mμ ($\epsilon = 3370$). Assuming that the compound in acidic solution existed completely in the phenazinone form, the absorption at 530 mμ could be used to measure the amount of phenazinone (XVII) present in equilibrium in water solutions of different concentrations. Because of the high absorbance exhibited by the solutions studied, the differential method of measurement was applied. The reference cells were filled with alkaline solutions of phenazinone (XVII) of the same concentration, and the differential absorbance shown at 530 mμ was attributed to the presence of phenazinone (XVII) in equilibrium. The approximate ratio of phenazinone (XVII) to anion (XVI) in a saturated aqueous solution of 4-nitro-1(5H)-phenazinone (XVII) was 7:93; on 5-fold dilution the ratio dropped to 2:98, and on 10-fold dilution no detectable amount of XVII was found.

In the nitrations of 2-amino-, 2-N-methylamino-, and 1-amino-phenazines, the nitro groups entered the α-positions of the ring. No β-substituted products were isolated, although in each case the β-position of the ring was available. These results were in agreement with those observed for other electrophilic reactions in the phenazine series such as chlorination (14) and direct nitration (15) in which only α-substituted products were obtained. Such behavior provided confirmatory evidence for the theoretical predictions which had been based on molecular orbital calculations (16, 17).

NOTE ADDED IN PROOF: A. Gray and F. G. Holliman (Tetrahedron, **18**, 1095 (1962)) have claimed the preparation of 1-amino-4-nitro-, 1-hydroxy-4-nitro-, and 1,4-diaminophenazine. On the basis of our present work we suggest that these compounds actually are: 1-amino-2-nitro-, 1-hydroxy-2-nitro-, and 1,2-diamino-phenazine, respectively.

EXPERIMENTAL

The melting points were determined in a Gallenkamp melting point apparatus and are uncorrected. The analyses were carried out in the C. Daesslé Laboratory, Montreal. Infrared spectra were determined on a Perkin–Elmer Model 21 double-beam instrument equipped with a sodium chloride prism. The ultraviolet absorption spectra were measured by means of a Beckman recording spectrophotometer Model DK1. Neutral, activity I Woelm aluminum oxide was used for chromatography unless otherwise noted.

2-Nitraminophenazine (II, III) (2-Nitrimino-(10H)phenazinium Betaine)

2-Aminophenazine (I) (200 mg; m.p. 279°) was powdered and dissolved in concentrated sulphuric acid (2 ml). The brown solution was cooled to −50° and formed a thick paste. Nitric acid (0.073 ml; sp. gr. 1.42; 70% nitric acid) was added at once, and the reaction mixture was stirred for 1–2 minutes until an orange liquid had formed. The temperature rose to about −20°. The solution was poured onto crushed ice (12.5 g) and was stirred until the ice had melted. The orange precipitate which formed was filtered, and the wet solid cake was suspended in water (100 ml). The addition of concentrated ammonia (16 drops) effected solution of the solid material and brought the pH of the solution to 8.0. The solution was filtered through a sintered-glass plate, then was heated to 50°. On addition of aqueous acetic acid (1:1; 20 drops) to the filtrate, fine yellow needles (243 mg) separated from solution. A portion of this material (100 mg) was dissolved in water (200 ml) and ammonia (6 drops) at 75°. The hot solution was acidified with aqueous acetic acid (1:2; 15 drops). On gradual cooling, gold needles deposited, and were isolated. A yield of 98 mg of 2-nitraminophenazine monohydrate (II), m.p. 150–160° (explodes), was obtained. $\bar{\nu}_{max}^{KBr}$ 3540, 3400, 3200, 2700, 1515, 1315, 1300, 880, 835, 820, 765, 755, 745 cm^{-1}. Anal. Calc. for $C_{12}H_8N_4O_2.H_2O$: C, 55.80; H, 3.95. Found: C, 55.22; H, 4.16%.

2-Nitraminophenazine monohydrate (II) (100 mg) was ground and suspended in dry benzene (50 ml). The suspension was heated to 50° for 2 hours with occasional swirling, then approximately 35 ml of the benzene was distilled off under reduced pressure at a temperature not exceeding 50°. The solid 2-nitraminophenazine (III) (60 mg) was separated by filtration, m.p. 150–160° (decomp.). $\bar{\nu}_{max}^{KBr}$ 3100–2700, 1510, 1320, 1295, 880, 855, 830, 820, 790, 765, 750, 740 cm^{-1}. Anal. Calc. for $C_{12}H_8N_4O_2$: C, 59.98; H, 3.36; N, 23.33. Found: C, 59.56; H, 3.40; N, 23.35%.

2-Amino-1-nitrophenazine (IV)

2-Nitraminophenazine (II, III) (0.5 g) was added gradually to concentrated sulphuric acid (5 ml) which had been cooled to −40°. The thick paste was stirred continuously. When all the substance had dissolved, the viscous brown liquid was kept in an ice-water bath for 3 hours. The reaction mixture was diluted with ice water (200 ml), and the precipitate (90 mg) which formed was filtered. The acidic filtrate was heated to 60°, then neutralized with ammonia, yielding 390 mg of a yellow-green substance. The crude material (400 mg) was dissolved in chloroform (500 ml), and the solution was chromatographed on alumina (90 g). Elution with methanol–chloroform (1:21) provided 2-amino-1-nitrophenazine (IV) (344 mg), yellow needles, m.p. 264–265°. $\bar{\nu}_{max}^{KBr}$ 3430, 3290, 3170, 1520, 1280, 845, 835, 802, 795, 770, 755, 740 cm^{-1}. Anal. Calc. for $C_{12}H_8O_2N_4$: C, 60.00; H, 3.40; N, 23.30. Found: C, 60.25; H, 3.43; N, 23.53%.

1,2-Diaminophenazine (V)

A suspension of 2-amino-1-nitrophenazine (IV) (50 mg) in glacial acetic acid (9 ml) was prepared by grinding the substance with acid in a mortar. The suspension was diluted with water (1.5 ml), and zinc powder (excess) was added in three small portions at 30°. The mixture was shaken vigorously; the yellow suspension became orange-brown and formed a clear solution. The excess zinc was filtered off and washed with water (8 ml). The filtrate was made alkaline by the gradual addition of concentrated ammonia (50 ml), whereupon the liquid became purple and brown lustrous needles were deposited from solution. The mixture was refrigerated for 3 hours, then the crystalline product (41 mg) was isolated. This material after two sublimations (1 mm at 130–135°) provided 1,2-diaminophenazine (V), purple needles, m.p. 189–191°. $\bar{\nu}_{max}^{KBr}$ 3390, 3300, 3170, 825, 785, 755 cm^{-1}. Anal. Calc. for $C_{12}H_{10}N_4$: N, 26.64. Found: N, 26.68%.

2-Amino-1-nitrophenazine (IV) (17 mg) was suspended in methanol (5 ml) and reduced with hydrogen in the presence of Adams' catalyst (14 mg PtO_2). The suspended particles dissolved and color changes from brown to purple to almost colorless were observed. The colorless solution on exposure to air became purple again and on evaporation of the solvent 13 mg of a brown solid was obtained. Sublimation of this material provided 1,2-diaminophenazine (V) in the form of purple needles.

2-Hydroxy-1-nitrophenazine (VI)

2-Amino-1-nitrophenazine (IV) (50 mg) was refluxed with 0.8% sodium hydroxide solution (25 ml). After 40 minutes, the solid dissolved, forming an orange solution. Refluxing was continued for 1 hour. The hot solution was filtered and treated dropwise with 3.7% hydrochloric acid at 60° until the pH was 2.0. Yellow crystals precipitated and, after standing overnight in a refrigerator, were filtered and washed with slightly acid water. The material was dissolved in hot water (20 ml) to which concentrated ammonia (4 drops) had been added. The orange solution was filtered hot and acidified to pH 2.0 by the dropwise addition of 3.7% hydrochloric acid at 80°. After standing overnight, the yellow needles which had precipitated were isolated. A yield of 46 mg of 2-hydroxy-1-nitrophenazine (VI), m.p. 238, was obtained. $\bar{\nu}_{max}^{KBr}$ 3040, 1550, 1530, 1250, 840, 802, 755 cm^{-1}. Anal. Calc. for $C_{12}H_7N_3O_3$: C, 59.75; H, 2.93; N, 17.42. Found: C, 59.67; H, 3.29; N, 17.49%.

2-Amino-1-nitrophenazine (IV) (22 mg) was dissolved in concentrated hydrochloric acid (15 ml). The solution was refluxed for 24 hours, during which time the liquid changed in color from red to orange to deep brown. It was filtered and ammonia was added to the hot filtrate until the pH was 3.0. The yellow needles (6 mg) which precipitated were isolated and identified as starting material (IV). After 2 days' standing at

room temperature, an orange crystalline substance precipitated from solution. This material was isolated and identified by its infrared spectrum as 2-hydroxy-1-nitrophenazine (VI), m.p. 223°.

2-N-Methylaminophenazine (VIII)

Methylaniline hydrochloride (1.45 g) and *o*-nitroaniline (1.40 g) were heated together. The mixture melted at 80–90°; at 135° fused zinc chloride (4.5 g) was added and the temperature was raised to 170° during ½ hour. A vigorous reaction ensued, with vapors of water and *o*-nitroaniline being evolved. The reaction subsided after a few seconds but the mixture was stirred at 170° for 25 minutes longer. Hot water (20 ml) was added carefully and stirring was continued until the mixture had cooled to room temperature. The aqueous layer was decanted, and the tarry residue was washed twice with water (3 ml), then was ground with 2% hydrochloric acid (20 ml). The acidic extract was filtered and the residue on the filter was washed with 0.5% hydrochloric acid. The combined filtrates were cooled and made alkaline with 20% sodium hydroxide (20 ml). A voluminous brown precipitate formed, which, after standing overnight, was filtered and washed with water until the latter gave a neutral reaction. The brown powder (1.2 g) was sublimed. At a temperature up to 120° under reduced pressure, unchanged *o*-nitroaniline was obtained; *in vacuo* with the temperature being gradually raised to 160°, an orange sublimate (0.35 g) was collected. Several batches of the latter (1.2 g) were combined and resublimed. At 125–130°, a sublimate consisting of *o*-nitroaniline and an oily material was obtained, and at 150–160° a mixture of orange and deep red crystals (0.77 g) sublimed. The latter mixture (1.76 g) was taken up in chloroform (176 ml) and filtered, leaving a residue (0.16 g) of 2-aminophenazine (I). The filtrate was chromatographed on alumina (450 g). Elution with chloroform provided 1.43 g of orange needles. Purification of these by sublimation afforded 2-N-methylaminophenazine (VIII), m.p. 199–201°. $\bar{\nu}_{max}^{KBr}$ 3260, 855, 815, 805, 755, 750, 735 cm^{-1}. Anal. Calc. for $C_{13}H_{11}N_3$: C, 74.62; H, 5.30; N, 20.08. Found: C, 74.73; H, 5.64; N, 20.16%. On further elution, 2-aminophenazine (I) (90 mg) was recovered.

2-N-Acetyl-N-methylaminophenazine (IX)

2-N-Methylaminophenazine (VIII) (100 mg) was dissolved in glacial acetic acid (0.5 ml), and acetic anhydride (0.5 ml) was added. The solution was allowed to remain at room temperature for 24 hours, then was diluted with water (2 ml) and evaporated to dryness under reduced pressure. Recrystallization of the residue from aqueous ethanol provided 2-N-acetyl-N-methylaminophenazine (IX) (75 mg), m.p. 155°. $\bar{\nu}_{max}^{KBr}$ 2980, 2900, 1665, 860, 830, 765, 760, 745 cm^{-1}. Anal. Calc. for $C_{15}H_{13}N_3O$: N, 16.69. Found: N, 16.78%.

2-N-Methylamino-1-nitrophenazine (X)

2-N-Methylaminophenazine (VIII) (200 mg) was dissolved in concentrated sulphuric acid (2 ml). The brown solution was cooled to −50° and solidified to a paste. Nitric acid (0.11 ml; sp. gr. 1.42) was added at once, and the mixture was stirred until a red liquid was obtained (10–20 seconds). The liquid was poured onto crushed ice (12.5 g), and the brown solution which formed was filtered. The filtrate was treated with ammonia at 0° until the pH was 3.0–4.0. A brown mass precipitated; it was filtered and washed with water until the wash water gave a neutral reaction. The crude product (200 mg) was taken up in chloroform (45 ml) and chromatographed on alumina (80 g). Elution with methanol–chloroform (1:20) and recrystallization from chloroform gave 162 mg of 2-N-methylamino-1-nitrophenazine (X), m.p. 278–280°. The analytical sample was sublimed *in vacuo* at a temperature above 200°. $\bar{\nu}_{max}^{KBr}$ 3340, 2900, 1515, 1265, 830, 802, 800, 785, 760 cm^{-1}. Anal. Calc. for $C_{13}H_{10}N_4O_2$: N, 22.04. Found: N, 22.14%.

1-Aminophenazine (XI)

Crude 2,2′-diaminodiphenylamine (m.p. 85–90°) (20 g) was heated and stirred with nitrobenzene (200 ml). A stream of nitrogen (3 bubbles/sec) was passed through the reaction vessel during the process. The reaction was controlled in such a way that as the nitrobenzene slowly distilled off, it was replaced continuously by the addition of fresh nitrobenzene (Table I). When the reaction was complete after 5 hours, the product (150 ml) was diluted with benzene (850 ml) and shaken with 3.7% hydrochloric acid (500 ml). The emulsion which formed was filtered and the residue was washed with the same acid (200 ml). The blue acidic layer of the combined filtrates was separated from the brown benzene layer, and the latter was extracted twice with the acid (300 ml). The combined acidic extracts (1 l.) were filtered, diluted with water (1 l.), and boiled

TABLE I

Progress of the oxidation reaction of 2,2′-diaminodiphenylamine with nitrobenzene

Time, hr	Amount of nitrobenzene, distilled off, ml	Amount of fresh nitrobenzene added, ml	Appearance of distillate
1	40	40	Yellow, cloudy
2	55	40	Orange, cloudy
3	48	40	Orange, slightly turbid
4	55	40	Orange, clear
5	52	40	Orange, clear

until no odor of nitrobenzene could be detected. Then the liquid (1.2 l.) was cooled and filtered. The gradual addition of anhydrous sodium acetate (150 g), with stirring, at room temperature, resulted in the formation of a precipitate. After standing for 3 hours in the refrigerator, the solid product was isolated. The red crystalline material (9.7 g) was sublimed twice, providing 1-aminophenazine (XI) (7.76 g), red crystals, m.p. 181–182°. Reported m.p. 179–181° (18). $\bar{\nu}_{max}^{KBr}$ 3480, 3340, 820, 765, 735 cm^{-1}.

1-Amino-4-nitrophenazine (XIV)

1-Aminophenazine (XI) (600 mg; m.p. 181–182°) was ground and dissolved in concentrated sulphuric acid (6 ml). The solution was cooled to a paste (−50°) and nitric acid (0.324 ml; sp. gr. 1.42) was added with stirring. The mixture was placed in an ice-water bath and stirring was continued for approximately 2 minutes until a drop of the liquid nitration mixture when added to ice water dissolved to form a yellow solution. Then the nitration mixture was poured onto crushed ice (300 g). The yellow suspension obtained was extracted with four portions of chloroform, the temperature being maintained near 0°. The chloroform extracts were combined (400 ml) and allowed to pass through a column of alumina (500 g; activity IV). Elution with chloroform provided a brown solution (600 ml) from which, on evaporation, was obtained 320 mg of 1-amino-4-nitrophenazine (XIV), orange needles, m.p. 281–282° (sublimes). $\bar{\nu}_{max}^{KBr}$ 3430, 3290, 1520, 1285, 820, 802, 775, 770, 765 cm^{-1}. Anal. Calc. for $C_{12}H_8O_2N_4$: N, 23.30. Found: N, 23.11%. Concentration of the mother liquor provided an additional 17 mg of (XIV), m.p. 274–278°, and when the mother liquor from this material was rechromatographed on alumina a further 7 mg of (XIV), m.p. 278–281°, was collected. In the latter instance, evaporation of the mother liquor to dryness left 95 mg of a brown crystalline powder, m.p. 140–145° (decomp.), which was distinguished by a strong band at 2150 cm^{-1} in the infrared spectrum.

4-Nitro-1(5H)-phenazinone (XVII)

1-Amino-4-nitrophenazine (XIV) (200 mg; m.p. 281–282°) was refluxed with a 1% solution of sodium hydroxide (80 ml). The solid dissolved completely after 20 minutes and the brown solution which formed was refluxed for another hour, then was allowed to cool slowly for 2 hours. A yellow precipitate settled out of solution, then redissolved when the mixture was heated to 60°. The hot liquid was filtered and the filtrate was acidified at room temperature to pH 2.0 by the dropwise addition of 3.7% hydrochloric acid. After standing for 3 hours at room temperature, the red crystalline material (180 mg) which formed was isolated. The latter (75 mg) was heated to 40° with water (150 ml), cooled to room temperature, and filtered. The filtrate was acidified with 3.7% hydrochloric acid (15 ml) at room temperature, and allowed to stand; a red crystalline substance precipitated and was isolated. A yield of 60 mg of 4-nitro-1(5H)-phenazinone (XVII), m.p. 200° (decomp.), was obtained.

1-Hydroxy-4-nitrophenazine Ammonium Salt (XVI)

Crude 4-nitro-1(5H)-phenazinone (XVII) (50 mg) was dissolved in water (20 ml) and rendered alkaline with ammonia (3 drops). The solution was filtered and treated with concentrated ammonia (14 drops) at 60°. The mixture was allowed to stand overnight in the refrigerator. Isolation of the precipitate which formed afforded 1-hydroxy-4-nitrophenazine ammonium salt (XVI) (22 mg) as light yellow needles, which decomposed at 280°. $\bar{\nu}_{max}^{KBr}$ 3400, 3100, 1540, 1530, 1510, 1320, 1265, 820, 805, 765 cm^{-1}. Anal. Calc. for $C_{12}H_{10}N_4O_3$: N, 21.70. Found: N, 21.45%.

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