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PHENAZINES—V

THE SYNTHESIS OF 2-AMINOPHENAZINE-1-CARBOXYLIC ACID*

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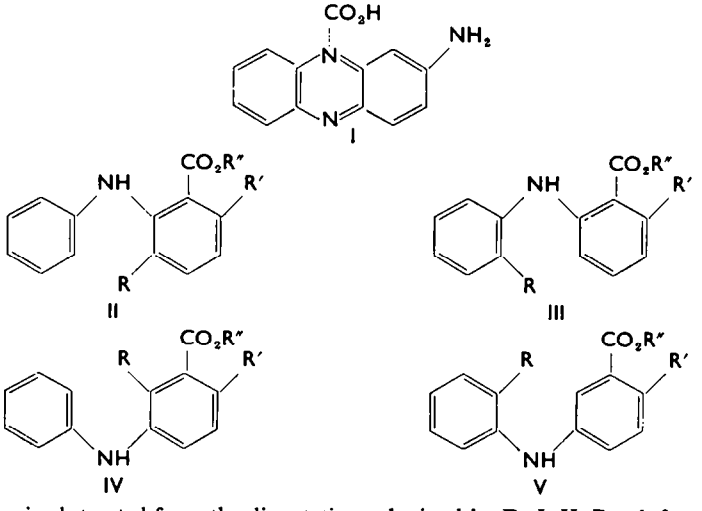
Abstract—2-Aminophenazine-1-carboxylic acid has been obtained from the ester which resulted from the oxidative cyclization in boiling nitrobenzene of the methyl esters of both 2,4-diaminodiphenylamine-3- and 2',3-diaminodiphenylamine-2-carboxylic acids. The acid was also prepared via the very unreactive nitrile, the latter being obtained from 2-amino-1-bromophenazine which was produced by the direct bromination of 2-aminophenazine.

THE syntheses of six of the seven possible 2-aminophenazine carboxylic acids have been reported,[1,2] This paper describes three routes by which the remaining isomer, 2-aminophenazine-1-carboxylic acid (I), has been prepared.

The most valuable method for synthesizing 2-aminophenazines appears to be through the nitrobenzene oxidation of suitable diaminodiphenylamines with one amino group in the 2 position,[3] a method which, already or indirectly, has given the six 2-aminophenazine carboxylic acids directly described.[1,2] In general, four 2-aminodiphenylamines may give rise to a particular phenazine, although not necessarily uniquely. Thus, 2-aminophenazine-1-carboxylic acid (I) might be expected from II, III, IV and V (R = R' = NH_2; R'' = H). Of these, V would be expected to give a mixture of the required compound with 3-aminophenazine-2-carboxylic



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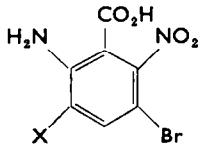
[1] F. G. Holliman, B. A. Jeffery and D. J. H. Brock, *Tetrahedron*, Part III, **19**, 1841 (1963).
[2] D. J. H. Brock and F. G. Holliman, *Tetrahedron*, Part IV, **19**, 1903 (1963) (previous paper).
[3] A. Gray, G. Gaertner and F. G. Holliman, *Tetrahedron* **18**, 1105 (1962).

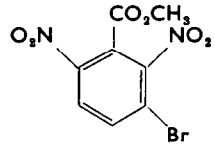
acid. Both II and III, with the carboxyl group in the 2 position, might give rise to acridones,[2] and III might also suffer extrusion of the carboxyl group during cyclization[4] giving 1-aminophenazine, although these side reactions could probably be avoided by cyclization of the methyl ester rather than the acids themselves. On the other hand, IV should give the required phenazine directly and our first approach was by this route.

The synthesis of a suitable intermediate, 5-bromo-6-nitroanthranilic acid (VI, X = H) has recently been described.[5] We found it necessary to use modified conditions for the conversion of 3-nitrophthalamic acid to 6-nitroanthranilic acid as the reported method[6] was particularly sensitive to the purity of the amide. Further, in our hands the bromination of 6-nitroanthranilic acid gave substantial amounts of a dibrominated derivative, probably VI (X = Br), in addition to the reported monobromo compound; bromination of the methyl ester gave only the dibrominated product even when the amount of bromine was restricted.

Attempts to condense 5-bromo-6-nitroanthranilic acid with aniline were unsuccessful. To enhance the reactivity of the halogen atom towards nucleophilic displacement, the amino group of methyl 5-bromo-6-nitro-anthranilate was oxidized to a



VI



VII

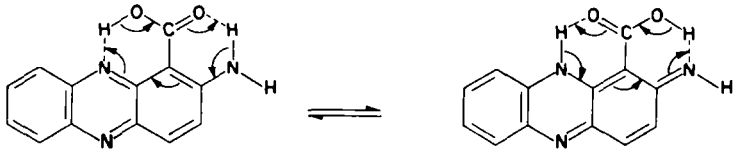
nitro group by the method of Holmes and Bayer,[7] the prior esterification serving to increase the bulkiness of the group *ortho* to the amino group in the hope that the competitive oxidation to the azoxy compound[8] would be reduced to a minimum. The ensuing methyl 3-bromo-2,6-dinitrobenzoate (VII) condensed smoothly and quantitatively with aniline to give the required diphenylamine (IV, R = R′ = NO_2, R″ = CH_3). This was reduced to the diaminodiphenylamine, oxidative cyclization of which led to a complex mixture of products from which methyl 2-aminophenazine-1-carboxylate was isolated by chromatography on alumina. The ester proved difficult to purify and was converted to the acid, the hydrolysis being carefully performed to minimize decarboxylation, to which the acid was prone. This ready decarboxylation, following partial hydrolysis of the ester in the nitrobenzene reaction mixture, accounted for the presence of 2-aminophenazine among the products of the oxidative cyclization.

The acid, like the other three 2-aminophenazine carboxylic acids with the carboxyl group adjacent to a ring nitrogen, was crystalline and readily recrystallized from aqueous ethanol, a solvent in which all the other isomers showed only slight, if any, solubility. Unlike the other six 2-aminophenazine carboxylic acids which gave the red-purple solutions in dilute acid typical of the 2-aminophenazinium chromophore, the new acid gave yellow solutions; the ester was also yellow, with a brilliant yellow

[4] G. Gaertner and F. G. Holliman; R. B. Herbert and F. G. Holliman, to be published.
[5] J. L. E. Erickson, J. M. Dechary and T. R. Pullig, *J. Amer. Chem. Soc.* **74**, 5622 (1952).
[6] R. Kahn, *Ber. Dtsch. Chem. Ges.* **35**, 3857 (1902).
[7] R. R. Holmes and R. P. Bayer, *J. Amer. Chem. Soc.* **82**, 3454 (1960).
[8] K. M. Ibne-Rasa and J. O. Edwards, *J. Amer. Chem. Soc.* **84**, 763 (1962).

fluorescence and was more soluble in water than the acid itself. That the compound isolated was, in fact, a 2-aminophenazine carboxylic acid, was shown by ready decarboxylation to 2-aminophenazine.

It seemed possible that this isomer would have other unique properties which warranted investigation in relation to the interesting feature of its structure (VIII a, b) allowing the intramolecular transfer of a proton; a structural feature of this type has been discussed by Cairns-Smith.[8] The yield in the above cyclization was very small and more attractive syntheses were sought.

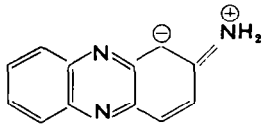


VIIIa VIIIb

In an attempt to shorten the route, the methyl ester of 6-nitroanthranilic acid was condensed with *o*-iodonitrobenzene to give methyl 2′,3-dinitrodiphenylamine-2-carboxylate (III, R = R′ = NO_2. R″ = CH_3). This condensation was best performed by a short period, high-temperature fusion of the reactants in the presence of potassium carbonate; even so, the yield of diphenylamine was small and the technique was only suited to small scale runs. An attempt to avoid this bottleneck by reducing methyl 6-nitroanthranilate to methyl 2,6-diaminobenzoate was foiled by the marked instability of the diamino ester under oxidizing conditions or in polar solvents, although, unlike the parent acid,[10] it is stable in the solid state at room temperature.

The dinitrodiphenylamine ester (III, R = R′ = NO_2, R″ = CH_3) was reduced to the diaminodiphenylamine which, on oxidative cyclization, gave again the methyl ester of 2-aminophenazine-1-carboxylic acid. The presence of both 1- and 2-aminophenazine in the reaction product indicated that some hydrolysis of the ester, followed by decarboxylation of the free acid to 2,3′-diaminodiphenylamine, was occurring in the nitrobenzene medium. Unfortunately, this route also gave a poor yield.

A third approach to the synthesis of the required compound was based upon the anticipation that the easily prepared 2-aminophenazine[9] would prove susceptible to electrophilic attack in the 1-position. This follows from the possibility of localizing a negative charge at C_1 in the activated state whilst leaving the adjacent quinoxaline system intact, e.g. IX. 2-Methoxyphenazine was brominated in the 1-position[11] and, under similar conditions, 2-aminophenazine gave 1-bromo-2-aminophenazine.*



IX

* 2-Nitroaminophenazine has recently been shown to rearrange to 2-amino-1-nitrophenazine.[13]

[9] A. G. Cairns-Smith, *J. Chem. Soc.* 182 (1961).

[10] C. M. Moser and T. Gompf, *J. Org. Chem.* **15**, 583 (1950).

[11] I. Yoshioka and S. Arafune, *Chem. Pharm. Bull., Tokyo* **7**, 581 (1959); *Chem. Abstr.* **54**, 17403 (1960).

[12] C. Stammer and A. Taurins, *Canad. J. Chem.* **41**, 228 (1963).

Exchange of the halogen atom with lithium could not be effected, unreacted starting material being recovered. As 1-bromo-2-hydroxy- and -2-methoxynaphthalenes both undergo the exchange reaction readily,[13] it seems likely that the heterocyclic system is responsible for the deactivation. Apart from electronic influences, it is likely that steric factors are also involved; addition of butyllithium across the azine system, as occurs with phenazine itself,[14] together with metalation of the amino group, might effectively block any approach to the bromine atom.

Fusion with anhydrous cuprous cyanide led to the replacement of the halogen atom by the cyanide group, offering an alternative route to the acid. The cyanide, which is effectively di-*ortho* substituted, proved extremely resistant to hydrolysis, a process which was further complicated by the ready decarboxylation of 2-aminophenazine-1-carboxylic acid under both acid and alkaline conditions. Conversion of the cyanide to the amide was achieved with alkaline hydrogen peroxide, and, although the amide in turn could not be hydrolysed, it could, unlike the cyanide, be converted to methyl 2-aminophenazine-1-carboxylate by methanolysis. Thus, the entry of the bromine atom to the 1-position of 2-aminophenazine was established.

The extended sequence of reactions necessary for the conversion of the cyanide to the acid with marked losses at each step meant that the overall yield of the required phenazine carboxylic acid was again low.

The properties of this acid will be discussed with those of the other members of the series in a later paper.

EXPERIMENTAL

M.ps. are uncorrected. Pet. ether refers to the fraction boiling 100–120°. Chromatographic alumina was Peter Spence grade 0. Chromatographic solvents were: A, butanol–conc HCl (4:1 saturated with water); B, butanol–acetic acid–water (4:1:5); C, butanol–formic acid–water (95:5, saturated with water); D, butanol saturated with 1·5 N ammonia.

6-Nitroanthranilic acid. Finely powdered 3-nitrophthalamic acid[10] (26 g) was added in one portion to a solution of bromine (7·5 cc) in 2 N NaOH (250 cc) cooled to −5°. Vigorous shaking dissolved the solid within 5 min and the solution was heated immediately to boiling. A brick red colour developing before the b.p. was reached indicated the success of the reaction. The solution was rapidly cooled to 0° and acidified with 5 N HCl with cooling and vigorous stirring. 6-Nitroanthranilic acid (16·8 g, 77%) was collected and recrystallized (water) to give yellow needles, m.p. 176–178° (lit 180°[6]).

Bromination of 6-nitroanthranilic acid. Bromine (1 cc) in acetic acid (8 cc) was added to a suspension of 6-nitroanthranilic acid (3·45 g) in glacial acetic acid (47 cc) at 15° with rapid stirring. Addition of sodium acetate trihydrate (2·7 g) in water (4 cc) gave a clear red solution which was poured on a mixture of ice (40 g) and water (160 cc). The precipitate was collected and, combined with that obtained by evaporation of an ethereal extract of the filtrate, was dissolved in hot 0·5 N NaOH (125 cc).

The solid (A) separating on cooling was filtered off and the filtrate acidified with 2 N HCl. Two recrystallizations of the precipitate from aqueous ethanol (charcoal) gave 5-bromo-6-nitroanthranilic acid (2·15 g, 44%), m.p. 198–200° (lit 201–202·5[5]).

The solid (A) was dissolved in boiling water, and the solution was filtered and acidified. The precipitated acid was reconverted to the sodium salt and recrystallized from water. Liberation of the acid and recrystallization (aqueous ethanol) gave a dibromo derivative (0·2 g), m.p. 229–230° (dec) (Found: C, 25·0; H, 1·7; N, 8·1; Br, 46·5. $C_7H_4Br_2N_2O_4$ requires: C, 24·7; H, 1·2; N, 8·2; Br, 47·1%) which was assumed to be 3,5-*dibromo-6-nitroanthranilic acid.*

Bromination of methyl 6-nitroanthranilate. Bromine (0·4 cc, 0·008 mole) in acetic acid (5 cc) was

[13] S. V. Sunthankar and H. Gilman, *J. Org. Chem.* **16**, 8 (1951).

[14] B. M. Mikhailov and A. N. Blokhina, *Izvest. Akad. Nauk. S.S.S.R., Otdel. Khim. Nauk.* 304, (1950); *Chem. Abstr.* **44**, 9452 (1950).

added to a rapidly stirred solution of methyl 6-nitroanthranilate[15] (1·3 g, 0·007 mole) in acetic acid (30 cc). A fine precipitate which had formed during the addition was filtered off. The filtrate was poured on ice and the precipitate recrystallized (aqueous methanol) to give fine yellow needles (0·5 g. 36%), m.p. 121–124°, presumed to be *methyl 3,5-dibromo-6-nitroanthranilate* (Found: C, 27·2; H, 2·2; N, 7·8; Br, 45·6. $C_8H_6Br_2N_2O_4$ requires: C, 27·1; H, 1·7; N, 7·9; Br, 45·2%). Hydrolysis of this ester by refluxing in 3 N NaOH for 1 hr gave an acid m.p. 228–230° (dec) identical (mixed m.p) with the dibromo acid obtained by direct bromination of 6-nitroanthranilic acid.

The precipitate which had formed during the bromination was dissolved in water. The solution, treated with excess sodium acetate, yielded unchanged methyl 6-nitroanthranilate (m.p. and mixed m.p. 105–108°).

Methyl 5-bromo-6-nitroanthranilate. 5-bromo-6-nitroanthranilic acid (9·9 g) in ether (100 cc) was treated with excess ethereal diazomethane at 0°. Removal of the solvent and recrystallization of the residue (methanol) gave the *ester* (5·6 g, 53%) as yellow plates, m.p. 127–130°. (Found: C, 35·0; H, 2·75; N, 10·0; Br, 29·7. $C_8H_7BrN_2O_4$ requires: C, 34·9; H, 2·55; N, 10·2; Br, 29·1%).

Methyl 3-bromo-2,6-dinitrobenzoate. Methyl 5-bromo-6-nitroanthranilate (5·6 g) was heated at 70° for 5 hr in a mixture of acetic acid (175 cc), 30% hydrogen peroxide (40 cc) and conc H_2SO_4 (5 cc). During the course of the reaction the colour changed from yellow through bottle-green (nitroso stage) to deep orange. The solution was cooled, filtered from a small amount of orange precipitate, and the reddish filtrate largely decolourized by running through a bed of charcoal. It was poured on a mixture of ice (500 g) and water (500 cc) and the resulting precipitate recrystallized (aqueous methanol, charcoal) to give the *dinitro ester* (3·8 g, 61%) as pale yellow needles, m.p. 118°. (Found: C, 31·1; H, 1·85; N, 8·9; Br, 26·6. $C_8H_6BrN_2O_6$ requires: C, 31·4; H, 1·65; N, 9·2; Br, 26·2%).

The orange precipitate after recrystallization (acetic acid) had m.p. 249–252°. Analytical figures suggest that it is *dimethyl 4,4'-dibromo-3,3'-dinitroazoxybenzene-2,2'-dicarboxylate.* (Found: C, 33·6; H, 2·5; N, 9·8. $C_{16}H_{10}Br_2N_4O_9$ requires: C, 34·2; H, 1·8; N, 9·9%).

Methyl 2,4-dinitrodiphenylamine-3-carboxylate. Methyl 3-bromo-2,6-dinitrobenzoate (1·55 g) and redistilled aniline (30 cc) were heated at 100° for 3 hr. The solution was cooled and poured with stirring into precooled 5 N HCl (100 cc). Filtration gave the *diphenylamine ester* (1·5 g, 90%), orange needles, m.p. 131–135°. Chromatography of a benzene solution of the crude ester on alumina raised the m.p. to 136–139°, a value unchanged by recrystallization from aqueous alcohol, aqueous acetic acid or pet. ether (Found; C, 53·6; H, 3·55; N, 13·9. $C_{14}H_{11}N_3O_6$ requires: C, 53·0; H, 3·45; N, 13·2%). The crude material proved satisfactory for subsequent reductions.

Reduction of methyl 2,4-dinitrodiphenylamine-3-carboxylate and characterization of the diaminodiphenylamine. The ester (0·2 g) was hydrogenated in ethanol (PtO_2). The solution was filtered and the solvent evaporated (N_2 atm.). Acetic anhydride (1 cc) was added to the rapidly darkening residue and the flask swirled until the solution set solid. Recrystallization from a chloroform–pet. ether mixture gave grey-white micro needles of *methyl 2,4-diacetamido-diphenylamine-3-carboxylate*, m.p. 173–175°. (Found: C, 62·9; H, 5·65; N, 12·2. $C_{18}H_{19}N_3O_4$ requires: C, 63·4; H, 5·55; N, 12·3%).

2-Aminophenazine-1-carboxylic acid. Methyl 2,4-dinitrodiphenylamine-3-carboxylate (1·21 g) was reduced as above. The ethanolic solution was filtered into nitrobenzene (150 cc), the ethanol removed by distillation and the residual solution refluxed for 8·5 hr. The solvent was stripped *in vacuo*, the residue taken up in benzene and adsorbed on an alumina column (2 × 37 cm). Elution with ether revealed a complex mixture of products, the main band being recognizable by its brilliant yellow fluorescence under UV light. It was removed from the column in ether, the solvent evaporated and the residue refluxed in 2 N NaOH for 1 hr. This time was established by paper chromatography (solvents A, B, D) as giving the best compromise between hydrolysis of all the ester and decarboxylation of the resulting acid. The solution was filtered hot from the contaminating 2-aminophenazine, cautiously brought to pH 8 with 5N HCl and then to pH 5 with acetic acid. Recrystallization of the precipitate (aqueous ethanol) gave *2-aminophenazine-1-carboxylic acid* (0·107 g, 11%) as yellow orange needles, m.p. 274–276° (with decarboxylation). Changing the eluting solvent from ether, through acetone to water removed a further portion (0·036 g, 4%) of the acid from the column (Found: C, 64·7; H, 3·55; N, 17·6. $C_{13}H_9N_3O_2$ requires: C, 65·3; H, 3·75; N, 17·6%).

Decarboxylation of 2-aminophenazine-1-carboxylic acid. The acid (2 mg) and copper powder

[15] E. H. Huntress, E. R. Atkinson, E. A. Ham and M. S. Tibbetts, *J. Amer. Chem. Soc.* **75**, 743 (1953).

(0·4 mg) were refluxed in quinoline (0·2 cc) for 10 min. The solution was diluted with benzene, adsorbed on an alumina column and the main band was eluted with ether. It was identified as 2-aminophenazine by mixed m.p. (278–280°) and paper chromatography (solvents A, B, C).

Methyl 2,6-diaminobenzoate. Methyl 6-nitroanthranilate (3 g) in ethanol (50 cc) was hydrogenated [3 atm over 5% Pd–C (1·5 g)] until a colourless solution resulted. The solvent was removed in N_2 and the residue recrystallized (water; charcoal). *Methyl 2,6-diaminobenzoate* (1·45 g, 59%) separated as silver needles, m.p. 78–80°. (Found: C, 57·7; H, 6·0; N, 17·4. $C_8H_{10}N_2O_2$ requires: C, 57·8; H, 6·0; N, 16·9%). The ester proved stable over 2 yr when kept in a dry, stoppered container. Solutions in polar solvents rapidly darkened, a black oil separating.

Attempts to condense this diamino ester with *o*-iodonitrobenzene under a variety of conditions produced unworkable, dark, viscous oils.

Methyl 2',3-dinitrodiphenylamine-2-carboxylate. Methyl 6-nitroanthranilate (1 g), *o*-iodonitrobenzene (1·25 g), K_2CO_3 (1 g) and Cu powder (0·1 g) were pulverized together. The mixture, contained in a boiling tube, was plunged into an oil-bath at 200° and held there until the vigorous effervescence slackened (5–6 min). The powdered melt was extracted twice with boiling water (10 cc), and the residue recrystallized (acetic acid; charcoal) to give the *diphenylamine ester* (0·55 g, 34%) as yellow orange plates, m.p. 131–133° (Found: C, 52·9; H, 3·85; N, 13·1. $C_{14}H_{11}N_3O_6$ requires: C, 53·0; H, 3·45; N, 13·2%). Attempts to prepare larger batches led to considerably diminished yields and an impure product.

Reduction of methyl 2',3-dinitrodiphenylamine-2-carboxylate, characterization of the diaminodiphenylamine and its cyclization. The dinitrodiphenylamine (0·2 g) was hydrogenated in ethanol (PtO_2). The solution was filtered and the solvent removed under N_2. To the yellow oil remaining acetic anhydride (1 cc) was added and the mixture allowed to stand with intermittent shaking for 1 hr. Excess acetic anhydride was removed under red. press. The residue recrystallized (benzene–pet ether) to give white spangles of needles of methyl 2',3-*diacetamidodiphenylamine-2-carboxylate* m.p. 168–169° (Found: C, 63·1; H, 5·8; N, 12·3. $C_{16}H_{19}N_3O_4$ requires: C, 63·4; H, 5·55; N, 12·3%).

The dinitrodiphenylamine (0·6 g) was hydrogenated in ethanol, the solution filtered into nitrobenzene (75 cc) and the ethanol removed by distillation. 5% Pd–C (0·3 g) was added and the solution refluxed for 16 hr. The solution was filtered, the solvent stripped, the residue taken up in benzne and adsorbed on an alumina column (2 × 20 cm). Elution with ether revealed a number of bands, three of which were identified.

(1) A deep red band was removed from the column first. Evaporation of the solvent and recrystallization of the residue (aq. ethanol) gave bright red needles of 1-aminophenazine, m.p. 175–178°, undepressed on admixture with an authentic sample.[8]

(2) A band fluorescing bright yellow under UV light was collected next. The solvent was evaporated and the residue refluxed in 2N NaOH for 1 hr. The solution was diluted, filtered, cooled in ice and acidified with acetic acid. Recrystallization of the precipitate (aq. ethanol) gave 2-aminophenazine-1-carboxylic acid (25 mg, 5%), m.p. 274–276° (dec). IR spectrum (KCl disc), mixed m.p. and paper chromatographic examination (solvents A, B, D) established it to be identical to the acid obtained from the oxidation of methyl 2,4-diaminodiphenylamine-3-carboxylate.

(3) The residue remaining after removal of the solvent from the third, orange fraction was heated under reflux with 2N NaOH for 1 hr. The insoluble portion was dissolved in benzene and rechromatographed on alumina. This component (35 mg) had m.p. 274–275° and was shown to be 2-aminophenazine by mixed m.p. and paper chromatography.

2-Amino-1-bromophenazine. A solution of bromine (1·28 g) in acetic acid (9 cc) was added dropwise and with vigorous shaking to 2-aminophenazine (1·48 g) in acetic acid (30 cc). The precipitated hydrobromide was collected, dissolved in boiling water, and the solution was again filtered. The filtrate was made alkaline with 3N NaOH and the orange precipitate (1·55 g, 75%), m.p. 210–212°, was recrystallized (aq. ethanol) to give orange needles of *2-amino-1-bromophenazine*, m.p. 211–212° (Found: C, 52·7; H, 3·0; N, 15·2; Br, 28·8. $C_{12}H_8BrN_3$ requires: C, 52·6; H, 2·9; N, 15·3; Br, 29·2%).

Attempts to exchange the bromine atom with lithium by reaction of the bromophenazine (either dissolved in tetrahydrofuran or suspended in ether) with various proportions of ethereal n-butyllithium were unsuccessful. Unchanged material was recovered in each case.

2-Amino-1-cyanophenazine. 2-Amino-1-bromophenazine (0·8 g) and freshly prepared anhydrous cuprous cyanide (0·5 g) were refluxed for 30 min with vigorous stirring in quinoline (20 cc). The solution

was diluted with benzene, filtered and adsorbed on an alumina column (2 × 30 cm). Elution with ether removed an orange band of unreacted 2-amino-1-bromophenazine followed by a band of 2-aminophenazine and finally a brilliantly fluorescent yellow band. The solvent was removed from the last fraction and the residue recrystallized (benzene) to give 2-*amino*-1-*cyanophenazine* (0·370 g, 58%), yellow needles, m.p. 284–285° (Found: C, 71·1; H, 4·1; N, 24·6. $C_{13}H_8N_4$ requires: C, 71·0; H, 3·65; N, 25·4%). Condensations using larger quantities of reactants, direct fusion or the use of nitrobenzene as solvent gave considerably diminished yields.

Attempts to hydrolyse the cyanide were either ineffective (ethanolic NaOH at reflux temp) or caused decarboxylation (conc H_2SO_4–acetic acid at 150° or methanolic KOH at 190°). Alcoholysis (methanol–conc H_2SO_4 at 125°) was also unsuccessful.

2-*Aminophenazine*-1-*carboxamide*. Hydrogen peroxide (20 cc; 30%) was added carefully to 2-amino-1-cyanophenazine (0·6 g) in ethanol (140 cc) and 25% NaOH aq. (10 cc). The solution was heated slowly to 70°, and after 1 hr a further portion of H_2O_2 (20 cc) cautiously added. Heating was continued at 70° for a further 2 hr. The ethanol was removed under red. press and the residue was well washed with water. 2-*Aminophenazine*-1-*carboxamide* (0·235 g, 36%) thus obtained recrystallized (aq. ethanol) as red-orange needles (which became yellow on drying), m.p. 270° (Found: C, 65·8; H, 4·3; N, 23·8. $C_{13}H_{10}N_4O$ requires: C, 65·5; H, 4·2; N, 23·5%).

The amide was not hydrolysed by refluxing in NaOH aq. The use of 100% H_3PO_4 caused both hydrolysis and decarboxylation. Bouveault's[16] diazotization method gave what appeared to be 2-hydroxyphenazine-1-carboxylic acid.

Reaction of 2-*aminophenazine*-1-*carboxamide with methanol and sulphuric acid at* 140°. The amide (0·2 g) in abs. methanol (30 cc) and conc H_2SO_4 (0·07 cc) was heated in a sealed tube at 140° for 5 hr. The solution was filtered, the methanol was evaporated and the residue was taken up in water (10 cc). Adjustment of the pH to 8 with NaOH precipitated unchanged amide, while leaving the ester in solution. The filtrate was made strongly alkaline with NaOH and warmed at 100° for 1 hr. The solution was filtered hot, cooled in ice and the pH adjusted to 5 with HCl and acetic acid. The precipitate was dissolved in ammonia, filtered, cooled and acidified as before. Recrystallization of the precipitate (aq. ethanol) gave 2-aminophenazine-1-carboxylic acid (43 mg, 22%), m.p. 270–274° (dec). It proved identical [mixed m.p., paper chromatography (solvents A, B, D) and IR spectrum ($CHCl_3$ solution)] with the acids obtained through the oxidation of the *o*-aminodiphenylamines.

Attempts to esterify the acid with diazomethane gave a product which could not be purified. It had, however, identical paper-chromatographic behaviour to the esters obtained from cyclization of the diphenylamine esters and by alcoholysis of 2-aminophenazine-1-carboxamide.

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[16] M. L. Bouveault, *Bull. Soc. Chim.* (3), **9**, 370 (1893).