1001. *Arylhydroxylamines. Part II.*[1] *Phenylhydroxylamine-N- and -O-sulphonic Acids.*

By E. Boyland and R. Nery.

Phenylhydroxylamine with pyridine–sulphur trioxide and other sulphonating reagents yields phenylhydroxylamine-*N*-sulphonic acid and, under more drastic conditions, the *NO*-disulphonic acid. *N*-Acetyl- and *N*-benzyloxycarbonylphenylhydroxylamine give the corresponding *O*-sulphonic acids; acid hydrolysis or catalytic reduction gives phenylhydroxylamine-*O*-sulphonic acid which rearranges intramolecularly to *o*-aminophenyl hydrogen sulphate. The sulphonic acids have been isolated as their ammonium and potassium salts.

Aromatic hydroxylamines are intermediates in the metabolism of carcinogenic aromatic amines and are excreted as conjugates of glucuronic acid,[2] sulphuric acid,[3] or *N*-acetylcysteine.[4] They react *in vitro* with thiols to give, by rearrangement, aminoaryl sulphides.[1] Hydroxylamine sulphate with chlorosulphonic acid gives mainly hydroxylamine-*O*-sulphonic acid.[5] Although the naturally occurring mustard-oil glucosides, sinigrin and sinalbin,[6] are derivatives of hydroxylamine-*O*-sulphonic acid, the arylhydroxyamine-sulphonic acids appear not to have been described.

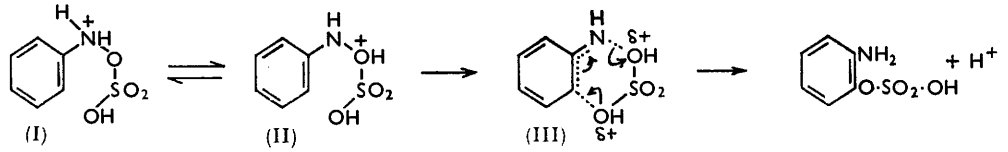
Equimolar quantities of phenylhydroxylamine with sulphur trioxide in nitromethane, pyridine–sulphur trioxide in a neutral organic solvent, or sulphamic or chlorosulphonic acid in pyridine give phenylhydroxylamine-*N*-sulphonic acid. Under more drastic conditions (an excess of sulphonating reagent, polar solvent, longer reaction time), the *NO*-disulphonic acid is formed. Similarly, *N*-substituted (*N*-acetyl, *N*-benzyloxycarbonyl) phenylhydroxylamines give the *N*-substituted *O*-sulphonic acids.

Ammonium and potassium salts of the various phenylhydroxylaminesulphonic acids were isolated as crystalline, water-soluble compounds, stable in the solid state in the absence of heat, light, and impurities and more stable in solution than is the parent hydroxylamine. They melt with sudden decomposition, giving tarry residues which contain aminophenols, azoxybenzene, and unidentified fluorescent products. They react slowly on chromatograms with suitable reagents (see Experimental) to give coloured derivatives, slowly oxidise iodide in acid solution, reduce ammoniacal silver nitrate and Fehling solution, and discharge the blue colour of the 4,5-dihydroxybenzene-1,3-disulphonic acid–ferric complex. They are unchanged in 2% aqueous sodium hydrogen carbonate or 2N-ammonia after 16 hours at room temperature in the dark, but decompose if these solutions are heated. In hot 2N-sodium hydroxide they give complex mixtures containing *o*- and *p*-aminophenol, aniline, azoxybenzene, and unidentified products. A solution of

[1] Part I, Boyland, Manson, and Nery, *J.*, 1962, 606.
[2] Cramer, Miller, and Miller, *J. Biol. Chem.*, 1960, **235**, 885; Miller and Miller, *Biochim. Biophys. Acta*, 1960, **40**, 380; Wyatt, Miller, and Miller, *Proc. Amer. Assoc. Cancer Res.*, 1961, **3**, 279.
[3] Boyland and Manson, unpublished work.
[4] Boyland, Manson, and Nery, unpublished work.
[5] Sommer, Schulz, and Nassau, *Z. anorg. Chem.*, 1925, **147**, 142; Sommer and Templin, *Ber.*, 1914, **47**, 1221.
[6] Ettlinger and Lundeen, *J. Amer. Chem. Soc.*, 1956, **78**, 4172.

N-benzyloxycarbonylphenylhydroxylamine-*O*-sulphonic acid in 10N-ammonia, after 20—30 minutes at room temperature, contains a mixture of *o*- and *p*-aminophenol, aniline, azoxybenzene, *o*- and *p*-aminophenyl sulphate, some starting material, and an unidentified substance. Since phenylhydroxylamine also gives the first four compounds under these conditions, it is likely that it is formed during the early stages of the alkaline hydrolysis of phenylhydroxylaminesulphonates.

Phenylhydroxylamine, *N*-acetylphenylhydroxylamine, and phenylhydroxylamine-*N*-sulphonic acid are converted by 2N-hydrochloric acid at room temperature into *p*-aminophenol; but *N*-benzyloxycarbonylphenylhydroxylamine, *N*-(phenylcarbamoyl)phenylhydroxylamine, and *N*-benzyloxycarbonylphenylhydroxylamine-*O*-sulphonic acid, under similar conditions, resist hydrolysis. The bulky *N*-substituents may hinder the approach of hydronium ions. The N–S bond is more acid-labile than the N–O bond: phenylhydroxylamine-*NO*-disulphonic acid in cold 2N-hydrochloric acid gives phenylhydroxylamine-*O*-sulphonic acid which then undergoes rearrangement and further hydrolysis (see below). Phenylhydroxylamine-*N*-sulphonic acid in 2N-hydrochloric acid yields *p*-aminophenol; the corresponding *O*-sulphonic acid yields mainly *o*-aminophenyl hydrogen sulphate and *o*-aminophenol. The *N*-sulphonic acid is probably hydrolysed to phenylhydroxylamine which undergoes intermolecular rearrangement by the mechanism postulated by Heller, Hughes, and Ingold;[7] the *O*-sulphonic acid may rearrange by an intramolecular mechanism through intermediate (III) formed from the reactive form (II) of (I).



The following findings are in agreement with these mechanisms: (*a*) Phenylhydroxylamine readily condenses with salicylaldehyde to give *N*-phenylsalicylaldehyde iso-oxime[8] which with hot aqueous potassium ferrocyanide gives a purple solution; this appears to be a specific reaction for aromatic hydroxylamines, since their acidic and alkaline decomposition products do not interfere.[9] On acid hydrolysis in the presence of salicylaldehyde, followed by neutralisation and heating with potassium ferrocyanide, phenylhydroxylamino-*N*-sulphonic acid gives this colour reaction; the corresponding *O*-isomer, or those compounds which yield it on hydrolysis (*N*-acetyl-, *N*-benzyloxycarbonyl-, and *N*-sulphophenylhydroxylamine-*O*-sulphonic acid) do not. (*b*) Catalytic reduction of *N*-benzyloxycarbonylphenylhydroxylamine-*O*-sulphonic acid yields phenylhydroxylamine-*O*-sulphonic acid, *o*-aminophenyl hydrogen sulphate, and *o*-aminophenol, but only traces of the *p*-aminophenyl derivatives. Phenylhydroxylamine-*O*-sulphonic acid in dry methanol containing hydrogen chloride yields mainly *o*-aminophenyl hydrogen sulphate; the *N*-sulphonic acid under similar conditions yields *p*-aminophenol and *p*-aminophenyl hydrogen sulphate. Compounds which yield the *O*-sulphonic acid on acid hydrolysis (cf. above) give mainly *o*-aminophenyl derivatives. (*c*) Treatment of phenylhydroxylamine or its *N*-sulphonic acid with phosphoric acid in aqueous methanol gives *p*-aminophenyl dihydrogen phosphate, but similar treatment of phenylhydroxylamine-*O*-sulphonic acid or its *N*-substituted derivatives (cf. above) gives no aminophenyl phosphates detectable by paper chromatography. (*d*) 2-Naphthylhydroxylamine-*O*-sulphonic acid, obtained as a metabolite of 2-naphthylamine, gives 2-amino-1-naphthyl hydrogen sulphate on mild acid treatment; 2-naphthylhydroxylamine, or its *N*-sulphonic acid, under similar conditions, gives 2-naphthylamine and 2-amino-1-naphthol.[3]

[7] Heller, Hughes, and Ingold, *Nature*, 1951, **168**, 909.
[8] Beckmann, *Annalen*, 1909, **367**, 275.
[9] Boyland and Nery, unpublished work.

Experimental

Paper Chromatography (see Table).—Unless otherwise stated, chromatograms were run on Whatman No. 1 filter paper in the following solvents: (A) butan-1-ol–propan-1-ol–ammonia (2N) (2 : 1 : 1); (B) butan-1-ol–acetic acid–water (10 : 1 : 2); and (C) butan-1-ol–propan-1-ol–water–pyridine (200 : 100 : 100 : 1). Phenylhydroxylamine and its derivatives were detected with (i) 1% of 4-dimethylaminocinnamaldehyde in ethanol–6N-hydrochloric acid (1 : 1), (ii) 0·5% ethanolic *p*-dimethylaminobenzaldehyde containing 1% of concentrated hydrochloric acid, (iii) 2% aqueous-ammoniacal silver nitrate (dark spots), (iv) 5% of potassium iodide in 0·5N-hydrochloric acid containing 1% of sodium starch glycollate (blue-purple spots), (v) 0·2% of " tiron " (4,5-dihydroxybenzene-1,3-disulphonic acid) in 0·05% aqueous ferric chloride (white—yellow spots on a blue background), or (vi) N-hydrochloric acid followed by 1% aqueous sodium nitrite and then, after 5—10 min., by 0·1% aqueous *N*-1-naphthylethylenediamine hydrochloride [for colours with (i), (ii), and (vi), see Table]. Sulphates and sulphonates were detected with (vii) Burma's sodium rhodizonate reagent [10] after treatment of chromatograms with 0·5N-hydrochloric acid and heating at 70° for 10—15 min.

R_F Values and colour reactions of phenylhydroxylamine and some of its derivatives.

	R_F values with solvent			Colour * with reagent		
Formula	A	B	C	(i)	(ii)	(vi)
$HO{\cdot}NPh{\cdot}SO_3NH_4$	0·28	0·22	0·26	m	y → br	p → bl-g
$HO{\cdot}NPh{\cdot}SO_3K$	0·26	0·20	0·23	m	y → br	p → bl-g
$KO_3S{\cdot}O{\cdot}NPh{\cdot}SO_3K$	0·05	0·02	0·05	m	y	bl-p
$Ac{\cdot}NPh{\cdot}O{\cdot}SO_3NH_4$	0·51	0·46	0·46	m	y → o	p
$Ac{\cdot}NPh{\cdot}O{\cdot}SO_3K$	0·47	0·43	0·41	m	y → o	p
$Ph{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}NPh{\cdot}OH$	0·92	0·88	0·90	p	y	—
$Ph{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}NPh{\cdot}O{\cdot}SO_3NH_4$	0·65	0·58	0·61	m	y	p
$Ph{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}NPh{\cdot}O{\cdot}SO_3K$	0·61	0·55	0·57	m	y	p
$Ph{\cdot}NH{\cdot}O{\cdot}SO_3K$	0·31	0·30	0·28	m	y	p
$Ph{\cdot}NH{\cdot}CO{\cdot}NPh{\cdot}OH$	0·94	0·89	0·90	p	y	r-br
$o\text{-}H_2N{\cdot}C_6H_4{\cdot}O{\cdot}SO_3K$	0·29	0·28	0·25	m	o	p-br
$p\text{-}H_2N{\cdot}C_6H_4{\cdot}O{\cdot}SO_3K$	0·17	0·10	0·15	r-br	o	bl-p
$PhNH{\cdot}OH$	0·92	—	0·94	p	o	bl-g

* y = Yellow, br = brown, m = mauve, p = purple, r = red, o = orange, g = green, bl = blue. For solvents and reagents, see text.

*Phenylhydroxylamine-*N*-sulphonic Acid.*—A solution of phenylhydroxylamine (15 g.) in chloroform (200 ml.) was stirred at 0° with pyridine–sulphur trioxide (14 g.). A colourless oil, which solidified after 30—40 min., separated after 5—10 min. After 3 hr. the solid was filtered off, washed with cold chloroform (25 ml.), dissolved in methanol (200 ml.), treated with dry ammonia at 0° until precipitation ceased, filtered off, and washed with cold methanol (50 ml.), and the combined filtrate and washings were evaporated *in vacuo* to about 20 ml. and diluted with cold ether until milky. This gave plates of *ammonium phenylhydroxylamine-*N*-sulphonate* (12 g.), m. p. 128° (decomp.) (Found: C, 35·5; H, 4·6; N, 13·3; S, 15·0. $C_6H_{10}N_2O_4S$ requires C, 35·0; H, 4·9; N, 13·6; S, 15·5%). A 10% w/v solution of the ammonium salt in methanol (20 ml.), on treatment with a similar solution (20 ml.) of potassium acetate, deposited plates of the *potassium sulphonate* (1·8 g.), m. p. 156° (decomp.) (Found: C, 31·6; H, 2·7; N, 6·1; S, 13·9. $C_6H_6KNO_4S$ requires C, 31·7; H, 2·7; N, 6·2; S, 14·1%). Phenylhydroxylamine also reacted with sulphamic or chlorosulphonic acid in pyridine, chloroform, or *NN*-dimethylaniline, and with gaseous sulphur trioxide in nitromethane, carbon tetrachloride, or ethylene dichloride, to yield phenylhydroxylamine-*N*-sulphonic acid. Attempts to isolate this substance by elution from charcoal or cellulose columns or by fractional crystallisation were unsuccessful.

*Phenylhydroxylamine-*NO*-disulphonic Acid.*—Attempts to prepare this compound by treating phenylhydroxylamine with 2·5 equivalents of pyridine–sulphur trioxide in chloroform for 17 hr. at room temperature gave only the mono-*N*-substituted derivative. A solution of phenylhydroxylamine (2 g.) in pyridine (20 ml.) containing pyridine–sulphur trioxide (6 g.) was stirred in the dark at room temperature for 16 hr. The precipitate obtained on addition of ether

[10] Burma, *Analyt. Chem.*, 1953, **25**, 549.

(100 ml.) was washed with ether (30 ml.), dissolved in methanol (50 ml.), and treated with dry ammonia at 0°, and the methanolic solution was then treated with potassium acetate as before, to yield rhombs of *dipotassium phenylhydroxylamine*-NO-*disulphonate* (0·3 g.), decomp. >150° (Found: C, 20·6; H, 1·9; N, 4·2; S, 18·3. $C_6H_5K_2NO_7S_2$ requires C, 20·8; H, 1·5; N, 4·1; S, 18·6%).

N-*Acetylphenylhydroxylamine*-O-*sulphonic Acid*.—Reaction of *N*-acetylphenylhydroxylamine (1 g.) and pyridine–sulphur trioxide (2 g.) in pyridine (20 ml.), after 16 hr. at 0°, and working up as in the preceding paragraph, gave *ammonium* N-*acetylphenylhydroxylamine*-O-*sulphonate* (0·7 g.), m. p. 122° (decomp.), as needles (Found: C, 38·8; H, 5·3; N, 11·1; S, 12·5. $C_8H_{12}N_2O_5S$ requires C, 38·7; H, 4·9; N, 11·3; S, 12·9%). A solution of the ammonium salt (0·4 g.) in ethanol (5 ml.), on treatment with 4% w/v potassium acetate in ethanol (10 ml.), gave the corresponding *potassium* O-*sulphonate* (0·4 g.), m. p. 151° (decomp.), as rhombs (Found: C, 35·4; H, 3·2; N, 5·6; S, 12·5. $C_8H_8KNO_5S$ requires C, 35·7; H, 3·0; N, 5·2; S, 11·9%).

N-*Benzyloxycarbonylphenylhydroxylamine*.—Benzyl chloroformate (15 g.) was added dropwise during 10 min. to a stirred solution of phenylhydroxylamine (20 g.) in chloroform (350 ml.). After 15 min. the mixture was placed over potassium hydroxide in a desiccator which was then evacuated so that the solution boiled gently for 1 hr. The precipitated phenylhydroxylamine hydrochloride was filtered off and washed with chloroform (100 ml.), and the combined chloroform solutions were evaporated *in vacuo* to about 80 ml. Light petroleum (b. p. 80—100°; 150 ml.) was added, giving N-*benzyloxycarbonylphenylhydroxylamine* (18 g.), m. p. 86°, as plates (Found: C, 69·1; H, 5·4; N, 5·8. $C_{14}H_{13}NO_3$ requires C, 69·1; H, 5·4; N, 5·8%). The reaction proceeded also in benzene or ether, but not in pyridine, *NN*-dimethylaniline, *NN*-dimethylformamide, or N-sodium hydroxide.

N-*Benzyloxycarbonylphenylhydroxylamine*-O-*sulphonic Acid*.—As in the preparation of phenylhydroxylamine-*N*-sulphonic acid, a solution of *N*-benzyloxycarbonylphenylhydroxylamine (3 g.) and pyridine–sulphur trioxide (3 g.) in pyridine (30 ml.), after 8 hr. in the dark at room temperature, gave *ammonium* N-*benzyloxycarbonylphenylhydroxylamine*-O-*sulphonate* (3·8 g.), m. p. 122° (decomp.), as needles (Found: C, 49·3; H, 4·8; N, 8·3; S, 9·4. $C_{14}H_{16}N_2O_6S$ requires C, 49·4; H, 4·7; N, 8·2; S, 9·4%). A solution of the ammonium salt (1 g.) in ethanol (15 ml.), on addition of 5% w/v potassium acetate in ethanol (15 ml.), deposited the corresponding *potassium* O-*sulphonate* (1 g.), m. p. 133° (decomp.), as needles (Found: C, 46·9; H, 3·6; N, 3·8; S, 8·4. $C_{14}H_{12}KNO_6S$ requires C, 46·5; H, 3·3; N, 3·9; S, 8·9%). *NN*-Dimethylaniline, but not chloroform, *NN*-dimethylformamide, or triethylamine, could be used in place of pyridine in this reaction.

O-*Acetylphenylhydroxylamine*-N-*sulphonic Acid*.—A suspension of ammonium phenylhydroxylamine-*N*-sulphonate (1 g.) in ether (25 ml.) was stirred at 0° with acetyl chloride (0·8 ml.) for 1 hr., the ether decanted, and the residue washed with ether (2 × 10 ml.), and dissolved in methanol (10 ml.). Paper chromatography revealed mainly decomposition products and a substance (R_F 0·50 and 0·42 in solvents A and B, respectively) which gave a positive sulphate reaction with reagent (vii) after acid-treatment and reacted slowly with reagents (i)—(vi) to give purple, orange, dark-grey, bluish-purple, white, and purple spots, respectively. Two-dimensional chromatography revealed that this substance, on treatment with 0·5N-hydrochloric acid gave *p*-aminophenol and inorganic sulphate, together with smaller amounts of *p*-aminophenyl hydrogen sulphate and *o*-aminophenol. It was also formed in small amounts in the reaction between ammonium phenylhydroxylamine-*N*-sulphonate and (*a*) acetic anhydride, (*b*) acetyl chloride in pyridine, or (*c*) thioacetic acid in pyridine or benzene, but the compound could not be isolated.

N-*Phenylcarbamoylphenylhydroxylamine*.—Prepared by Durand and Naves's method,[11] this had m. p. 134° (decomp.) (lit.,[11] m. p. 126°) (Found: C, 68·3; H, 5·2; N, 12·3. Calc. for $C_{13}H_{12}N_2O_2$: C, 68·4; H, 5·3; N, 12·3%). Attempts to prepare its *O*-sulphonic acid were unsuccessful.

Phenylhydroxylamine-O-*sulphonic Acid*.—Solutions of (*a*) potassium or (*b*) ammonium *N*-benzyloxycarbonylphenylhydroxylamine-*O*-sulphonate in (*c*) methanol or (*d*) ethanol containing (*e*) imidazole, (*f*) piperidine, (*g*) sodium hydrogen carbonate, (*h*) potassium acetate, or (*i*) acetic acid were catalytically hydrogenated in the presence of (*j*) 5% palladium–barium sulphate, (*k*) 5% palladium–charcoal, or (*l*) Adams catalyst. Hydrogen uptake in all solutions containing (*e*)—(*h*) was slow or negligible and only starting material was recovered in each case.

[11] Durand and Naves, *Compt. rend.*, 1925, **180**, 522.

A solution of (*a*) or (*b*) in (*c*) or (*d*) containing (*j*), (*k*), or (*l*) had an initially slow rate of hydrogen uptake, a gradual increase in acidity, and a corresponding increase in the rate of hydrogen uptake. There was a rapid uptake of 2 equiv. of hydrogen by all solutions containing acetic acid. All solutions in which reduction occurred contained inorganic sulphate and *o*-aminophenyl hydrogen sulphate.

A solution of the ammonium salt (*b*) (5 g., 14·7 mmoles) in methanol (250 ml.) containing palladium–charcoal (*k*) (0·2 g.) was hydrogenated for 1 hr., 13·2 mmoles of hydrogen being taken up. The mixture was filtered, the residue was washed with methanol (50 ml.), the combined filtrate and washings were treated with dry ammonia at 0°, the precipitate of ammonium sulphate was filtered off and washed with methanol (20 ml.), and the combined methanolic solutions were concentrated under reduced pressure to 5 ml. This residue was applied as streaks on sheets of 3 MM chromatography paper, run overnight in solvent C, strips (R_F 0·28—0·32) were cut off and eluted with methanol (200 ml.), and the eluates were concentrated *in vacuo* to 5 ml. and treated with a 5% w/v solution of potassium acetate in methanol (5 ml.), to yield *potassium phenylhydroxylamine*-O-*sulphonate* (0·1 g.), m. p. 170—174° (decomp.), as needles (Found: C, 31·8; H, 2·6; N, 5·8; S, 14·5%). Similar treatment of the strips (R_F 0·25—0·28 and 0·58—0·64) gave potassium *o*-aminophenyl sulphate (0·42 g.) and potassium *N*-benzyloxycarbonylphenylhydroxylamine-*O*-sulphonate (0·65 g.), respectively.

Attempts to convert salt (*a*) or (*b*) into phenylhydroxylamine-*O*-sulphonic acid by hydrolysis in (i) 10% hydrogen bromide in acetic acid, (ii) 2N- or (iii) 10N-ammonia, or (iv) 2N-hydrochloric acid, or by reduction in (v) ethanol–ammonia–hydrogen sulphide, (vi) zinc dust–dilute acetic acid, (vii) aqueous sodium dithionite, (viii) ferrous sulphate–dilute ammonia, or (ix) hydrazine–ethanol, either resulted in extensive decomposition in solutions (i), (iii), (viii), and (ix), or in little or no reaction in the others.

Acidic Hydrolysis of Phenylhydroxylamine and Some of its Derivatives.—(*a*) *In* 2N-*hydrochloric acid.* 10% w/v Solutions of the following compounds in 2N-hydrochloric acid were set aside at room temperature and samples removed after varying times, spotted on chromatography paper, neutralised with ammonia vapour, and run in solvents A and C: (1) potassium phenylhydroxylamine-*N*-sulphonate, (2) dipotassium phenylhydroxylamine-*NO*-disulphonate, (3) potassium *N*-acetylphenylhydroxylamine-*O*-sulphonate, (4) *N*-benzyloxycarbonylphenylhydroxylamine, (5) potassium *N*-benzyloxycarbonylphenylhydroxylamine-*O*-sulphonate, (6) *N*-acetylphenylhydroxylamine, (7) *N*-phenylcarbamoylphenylhydroxylamine, (8) potassium phenylhydroxylamine-*O*-sulphonate, and (9) phenylhydroxylamine. Compound (1) was completely hydrolysed after 40 min. to *p*-aminophenol and traces of *p*-aminophenyl hydrogen sulphate (but none of the *o*-isomer), *o*-aminophenol, and other products. Compounds (2) and (3) gave phenylhydroxylamine-*O*-sulphonic acid, and (2), (3), and (8) gave *o*-aminophenyl hydrogen sulphate and *o*(and a trace of *p*)-aminophenol. Compounds (4), (5), and (7) were unchanged after 40 min., but when heated at 70° for 20—30 min., all gave mixtures of *o*- and *p*-aminophenols and other products. Compounds (6) and (9) gave *p*(and a trace of *o*)-aminophenol.

(*b*) *In methanolic hydrogen chloride.* A solution of compound (8) in methanol, after treatment with dry hydrogen chloride at 0°, contained mainly *o*-aminophenyl hydrogen sulphate; compound (1), treated similarly, gave *p*-aminophenyl hydrogen sulphate and *p*-aminophenol.

(*c*) *In aqueous-methanolic phosphoric acid.* 1% w/v Solutions of compounds (1)—(9) in 2N-phosphoric acid in 50% methanol, after 2 hr. at room temperature, showed similar products as in (*a*), in addition to *p*-aminophenyl dihydrogen phosphate in cases (1), (6), and (9). This phosphate showed R_F values and colour reactions identical with those described by Boyland and Manson.[12]

Reaction of Phenylhydroxylamine and Some of its Derivatives with Salicylaldehyde.—0·005M-Solutions (5 ml.) of compounds (1)—(9) in N-hydrochloric acid, as in the foregoing experiment, were treated with 0·2% v/v salicylaldehyde in ethanol (5 ml.). Aliquot parts (2 ml.) were neutralised with 2N-ammonia after 1, 3, and 6 hr., severally, treated with 5% aqueous potassium ferrocyanide (0·1 ml.), heated at 70° for 10 min., cooled, and shaken with chloroform (2 ml.). Only compounds (1), (9) and, to a smaller extent, (6) gave a purple aqueous layer.

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[12] Boyland and Manson, *J.*, 1957, 4689.

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