597. *Substituent Interactions in* ortho-*Substituted Nitrobenzenes. Part IV.*[1]

By J. D. Loudon and G. Tennant.

Whereas ethereal hydrogen chloride causes an *o*-nitrobenzaldehyde to condense with ethyl acetoacetate or with phenol to form a chlorinated 1-hydroxyquinolone, *e.g.*, (I; R = Cl), or chlorinated anthranil, *e.g.*, (IV), respectively, ethereal hydrogen bromide often effects the reactions without entry of halogen into the product. Moreover, hydrogen chloride and ethyl α-2-nitrobenzylideneacetoacetate, which normally yield the chloro-1-hydroxyquinolone (I; R = Cl), yield the unchlorinated analogue (I; R = H) in presence of quinol. Quinol also reacts with *o*-nitrobenzaldehydes in presence of hydrogen chloride, giving 3-(2,5-dihydroxyphenyl)anthranils without entry of chlorine.

As was shown in Part III,[1] *o*-nitrobenzaldehyde condenses with ethyl acetoacetate in presence of hydrogen chloride forming the chloro-1-hydroxy-4-quinolone (I; R = Cl). It was therefore unexpected when an apparently comparable reaction, with hydrogen bromide as condensing agent, gave the halogen-free analogue (I; R = H) which had earlier been obtained by hydrogenolysis of the chloro-derivative (I; R = Cl). Some observations relating to this contrast in behaviour are reported here.

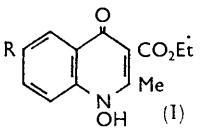
Condensation was effected by saturating an ethereal solution of the organic components with hydrogen chloride or bromide. The resultant precipitate, consisting of an unstable hydrohalide, afforded the 1-hydroxyquinolone when triturated with water or crystallised from hydroxylic solvents. With ethyl acetoacetate and 5-chloro-2-nitrobenzaldehyde hydrogen bromide gave the chloro-1-hydroxyquinolone (I; R = Cl) whereas hydrogen chloride gave the dichloro-compound (II). The structure of the latter product was established by hydrolysis followed by reduction and decarboxylation to 6,8-dichloro-4-hydroxyquinaldine (III) which was synthesised from 2,4-dichloroaniline.[2] In a similar way 5-bromo-2-nitrobenzaldehyde was condensed to the bromo-1-hydroxyquinolone (I; R = Br) by using hydrogen bromide or, by using hydrogen chloride, to a bromochloro-1-hydroxyquinolone. The latter was converted, by hydrogenolysis of the derived 1-*O*-acetate, into ethyl 4-hydroxyquinaldine-3-carboxylate and is assigned the 6-bromo-8-chloro-orientation by analogy with compound (II). 2-Nitroarylidene derivatives of ethyl acetoacetate are potential intermediates in these condensations and were sometimes isolated. Pre-formed ethyl α-2-nitrobenzylideneacetoacetate reacted with hydrogen bromide, giving the 1-hydroxyquinolone (I; R = H) or with hydrogen chloride giving the chloro-compound (I; R = Cl).

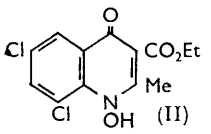
A halogen-free 1-hydroxyquinolone (I; R = H, Ac for CO_2Et) was likewise obtained when *o*-nitrobenzaldehyde was condensed with acetylacetone by means of hydrogen

[1] Part III, Loudon and Wellings, *J.*, 1960, 3470.
[2] Hughes and Lyons, *J. Proc. Roy. Soc. New South Wales*, 1938, **71**, 458.

bromide, or when this acid reacted with pre-formed 3-2′-nitrobenzylideneacetylacetone: the corresponding reactions with hydrogen chloride had given the 6-chloro-1-hydroxyquinolone (I; R = Cl, Ac for CO_2Et).[1] The relation between these two quinolones was confirmed by hydrogenolysis of their respective 1-*O*-acetates whereby in each case 3-acetyl-4-hydroxyquinaldine was formed.

o-Nitrobenzaldehyde is known to react with aromatic compounds under acidic conditions, affording different types of product including triarylmethanes,[3] anthranils,[4]


(I)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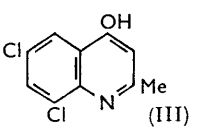
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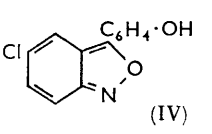
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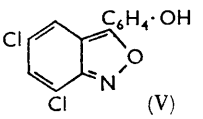
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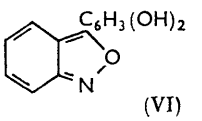
(VI)

and acridines.[5] As Zincke and Siebert showed [6] it reacts with phenol or *p*-cresol in hydrochloric–acetic acid to form 3-aryl-5-chloroanthranils, *e.g.*, (IV), of which the structure has been confirmed by Simpson and Stephenson [7] who used the compounds as sources of 2-aminobenzophenones through reduction with iron and acetic acid. A more recent claim [8] that 4′-hydroxy-2-nitrodiphenylmethanol (of m. p. 228—229°) is formed by the interaction of hydrogen chloride, phenol, and *o*-nitrobenzaldehyde in methanol requires substantiation. Attempts to repeat this experiment gave in our hands only the chloroanthranil (IV) (m. p. 240°) of which, it may be noted, the C- and N-analyses closely correspond with those for the alleged diphenylmethanol.

The points of resemblance between Zincke and Siebert's reaction and that leading to the 1-hydroxy-4-quinolones led us to compare the two reactions further and we first ascertained that the anthranil (IV) is also readily formed in ether instead of acetic acid as solvent. Investigation with phenol as fixed component then revealed for the anthranil reaction a similar, if less marked, difference in behaviour between hydrogen chloride and hydrogen bromide as condensing agents. Thus 5-chloro- and 5-bromo-2-nitrobenzaldehyde reacted in presence of hydrogen chloride to form 5,7-dichloro- and 5-bromo-7-chloro-3-*p*-hydroxyphenylanthranil, whereas in presence of hydrogen bromide they yielded 5-chloro- and 5-bromo-3-*p*-hydroxyphenylanthranil, respectively. However, from *o*-nitrobenzaldehyde and hydrogen bromide the product was a mixture of 3-*p*-hydroxyphenylanthranil and its 5-bromo-derivative.

The new anthranil derivatives were identified by analysis and through the products which they formed on reduction. Hydrogenation over palladium–charcoal in acetic acid afforded a common, halogen-free product with properties consistent with its formulation as 2-amino-4′-hydroxydiphenylmethane. On the other hand, sodium dithionite smoothly reduced the halogenated anthranils to halogenated 2-amino-4′-hydroxybenzophenones and oxidation of these, after protection of the amino-group, gave known derivatives of anthranilic acid. In this way degradation to *N*-acetyl-3,5-dichloroanthranilic acid established the substitution pattern of the anthranil (V).

[3] Tanasescu and Simonescu, *J. prakt. Chem.*, 1934, **141**, 311; Driver and Mok, *J.*, 1955, 3914.
[4] Kliegel, *Ber.*, 1908, **41**, 1845; 1909, **42**, 591.
[5] Albert, " The Acridines," Arnold and Co., London, 1951; Tanasescu, Ionescu, Goia, and Mantsch, *Bull. Soc. chim. France*, 1960, **4**, 698.
[6] Zincke and Siebert, *Ber.*, 1906, **39**, 1930.
[7] Simpson and Stephenson, *J.*, 1942, 353; cf. Simpson, Atkinson, Schofield, and Stephenson, *J.*, 1945, 646.
[8] Schultz and Geller, *Arch. Pharm.*, 1955, **288**, 234.

Because of its reducing properties quinol was next chosen as phenolic component of the anthranil reaction. Condensed with *o*-nitrobenzaldehyde in presence of hydrogen chloride it gave a halogen-free compound which on oxidation afforded anthranil-3-carboxylic acid and is thus regarded as 3-(2,5-dihydroxyphenyl)anthranil (VI). Similar condensations with 5-chloro- and 5-bromo-2-nitrobenzaldehyde, whether effected by hydrogen chloride or bromide, gave without entry of halogen the appropriate 5-halogeno-derivatives of the anthranil (VI). Rather surprisingly *o*-nitrobenzaldehyde in presence of hydrogen bromide formed a mixture of the anthranil (VI) and its 5-bromo-derivative.

The influence of quinol may also be enlisted in the quinolone series. Thus in its presence ethyl α-2-nitrobenzylideneacetoacetate was converted by hydrogen chloride into the halogen-free 1-hydroxyquinolone (I; R = H). Ethyl α-(5-chloro- and 5-bromo-2-nitrobenzylidene)acetoacetate likewise reacted forming the monohalogeno-hydroxyquinolones (I; R = Cl and Br, respectively). In absence of hydrogen chloride or when this was replaced by trichloroacetic acid no reaction occurred.

From these results it appears that in the course of this 1-hydroxyquinolone or anthranil synthesis there is involved a reduction step which can be effected by hydrogen bromide or by quinol but not by hydrogen chloride as reducing agent; the last reagent supplies the requisite accession of electrons to the nitro-group through entry of chloride ion into the nucleus (cf. Part III). The detailed steps, however, remain obscure. As a possible model we examined the action of the two hydrogen halides on *o*-nitrosobenzoic acid but the only products positively identified were 5-chloro- and 5-bromo-anthranilic acid, respectively. Further inquiry is in progress.

Experimental

Ethyl α-2-Nitrobenzylideneacetoacetate.—A mixture of *o*-nitrobenzaldehyde (3 g.), ethyl acetoacetate (2·7 g.), acetic anhydride (4·9 ml.), and potassium hydrogen carbonate (3 g.) was heated at 100° for 2 hr., then cooled and poured into water, and the whole was extracted with ether. The gum, recovered from the washed (sodium hydrogen carbonate, then water) and dried ($MgSO_4$) extract, gave the *ester*, m. p. 69° (from ethanol) (Found: C, 59·3; H, 5·1; N, 5·4. $C_{13}H_{13}NO_5$ requires C, 59·3; H, 5·0; N, 5·3%). Heller, Lauth, and Buchwaldt [9] describe the compound as an oil. The 5-chloro- and 5-bromo-derivatives were isolated incidentally to reactions described below.

1-Hydroxy-4-quinolones.—(*a*) The general procedure consisted in saturating with the hydrogen halide at 20° an ethereal solution containing equimolar proportions of the appropriate nitrobenzaldehyde and reactive methylene compound. Generally, within 24 hr., an unstable crystalline hydrohalide had separated from the (sealed) solution and after 48 hr. (with resaturation if necessary) this was collected, combined with a small second crop usually obtained from the partially evaporated mother-liquor, and it was treated with dilute sodium hydroxide (rather insoluble sodium salts may be formed). Acidification with dilute sulphuric acid afforded the 1-hydroxyquinolone (yields based on the aldehyde). In some cases complete evaporation of the residual reaction solution then gave the nitrobenzylidene compound which was purified by recovery from ether after being washed with dilute sodium carbonate. Such nitrobenzylidene compounds, treated with ethereal hydrogen halide, gave the appropriate 1-hydroxyquinolones when resubmitted to the foregoing treatment.

(*b*) Ethyl 1,4-dihydro-1-hydroxy-2-methyl-4-oxoquinoline-3-carboxylate (I; R = H), m. p. 175° (from ethanol) (Found: C, 63·2; H, 5·3; N, 6·0. Calc. for $C_{13}H_{13}NO_4$: C, 63·2; H, 5·3; N, 5·7%), was formed in 60% yield *via* the *hydrobromide*, m. p. 140° (from ethyl acetate–ethanol) (Found: C, 47·4; H, 4·0; N, 4·5. $C_{13}H_{14}BrNO_4$ requires C, 47·6; H, 4·3; N, 4·3%), from *o*-nitrobenzaldehyde, ethyl acetoacetate, and hydrogen bromide. It was also obtained from ethyl α-2-nitrobenzylidineacetoacetate (*a*) in ethereal hydrogen bromide (yield 60%), (*b*) in reaction (48 hr.) with quinol and hydrogen chloride in tetrahydrofuran (yield 90%). The hydrobromide, heated at 150° for 10 min., afforded the carboxylic acid [1] (I; R = H, CO_2H for CO_2Et), m. p. 215° (decomp.) (Found: C, 59·9; H, 4·1; N, 6·3. Calc. for $C_{11}H_9NO_4$: C,

[9] Heller, Lauth, and Buchwaldt, *Ber.*, 1922, **55**, 483.

60·2; H, 4·1; N, 6·4%), which was also prepared by saponifying the ester and was decarboxylated at 220° to 1,4-*dihydro*-1-*hydroxy*-2-*methyl*-4-*oxoquinoline*, m. p. 248° (from dimethylformamide) (Found: C, 68·8; H, 5·5; N, 7·5. $C_{10}H_9NO_2$ requires C, 68·6; H, 5·2; N, 8·0%).

(*c*) Ethyl 6-chloro-1,4-dihydro-1-hydroxy-2-methyl-4-oxoquinoline-3-carboxylate (I; R = Cl), identified with an authentic specimen [2] by its m. p. and infrared spectrum, was obtained (*a*) *via* its *hydrobromide*, m. p. 135° (decomp.) (from ethyl acetate–ethanol) (yield 45%) (Found: C, 43·1; H, 3·8; N, 4·1. $C_{13}H_{13}BrClNO_4$ requires C, 43·0; H, 3·6; N, 3·9%), from 5-chloro-2-nitrobenzaldehyde and ethyl acetoacetate in ethereal hydrogen bromide and (*b*) from ethyl α-2-nitrobenzylideneacetoacetate in ethereal hydrogen chloride (yield 73%). It was also obtained from ethyl α-(5-chloro-2-nitrobenzylidene)acetoacetate (cf. below) (i) (yield 80%) in ethereal hydrogen bromide and (ii) (yield 86%) in reaction with hydrogen chloride and quinol in tetrahydrofuran.

(*d*) *Ethyl* 6-*bromo*-1,4-*dihydro*-1-*hydroxy*-2-*methyl*-4-*oxoquinoline*-3-*carboxylate* (I; R = Br), m. p. 219° (from ethanol) (Found: C, 47·6; H, 3·8; N, 4·1. $C_{13}H_{12}BrNO_4$ requires C, 47·9; H, 3·7; N, 4·3%), was obtained (yield 40% after allowance for 20% recovery of aldehyde) from 5-bromo-2-nitrobenzaldehyde in ethereal hydrogen bromide, *via* the *hydrobromide*, m. p. 140° (from ethyl acetate–ethanol) (Found: C, 38·1; H, 3·2; N, 3·5. $C_{13}H_{13}Br_2NO_4$ requires C, 38·3; H, 3·2; N, 3·4%). It was also obtained from ethyl α-(5-bromo-2-nitrobenzylidene)-acetoacetate (cf. below) (*a*) (yield 70%) in ethereal hydrogen bromide and (*b*) (yield 82%) by reaction with hydrogen chloride and quinol in tetrahydrofuran. The 1-*acetoxy-compound*, m. p. 211° (from ethanol) (Found: C, 49·0; H, 3·8; N, 4·0. $C_{15}H_{14}BrNO_5$ requires C, 48·9; H, 3·8; N, 3·8%), afforded ethyl 4-hydroxyquinoline-3-carboxylate by hydrogenolysis over palladium–charcoal in ethanol.

(*e*) *Ethyl* 6,8-*dichloro*-1,4-*dihydro*-1-*hydroxy*-2-*methyl*-4-*oxoquinoline*-3-*carboxylate* (II), m. p. 203° (from ethanol) (yield 60%) (Found: C, 49·4; H, 3·8; N, 4·6. $C_{13}H_{11}Cl_2NO_4$ requires C, 49·4; H, 3·5; N, 4·4%), together with α-(5-*chloro*-2-*nitrobenzylidene*)*acetoacetate*, m. p. 101° (from ethanol; yield 30%) (Found: C, 52·4; H, 4·2; N, 4·7. $C_{13}H_{12}ClNO_5$ requires C, 52·4; H, 4·0; N, 4·7%), were obtained from 2-chloro-5-nitrobenzaldehyde and ethyl acetoacetate in ethereal hydrogen chloride. With warm acetic anhydride the dichlorohydroxyquinolone formed the 1-*acetoxy-compound*, m. p. 130° (from ethanol) (Found: C, 50·5; H, 3·8; N, 4·2. $C_{15}H_{13}Cl_2NO_5$ requires C, 50·3; H, 3·6; N, 3·9%) which, on hydrogenolysis over palladium–charcoal in ethanol, gave ethyl 4-hydroxyquinaldine-3-carboxylate, identified by mixed m. p. 228° and by its infrared spectrum.[1] Hydrolysis of the parent quinolone-ester in aqueous sulphuric–acetic acid gave the corresponding *carboxylic acid*, m. p. 258° (from dimethylformamide) (Found: C, 46·3; H, 3·0; N, 5·0. $C_{11}H_7Cl_2NO_4$ requires C, 45·8; H, 2·4; N, 4·9%).

6,8-*Dichloro*-4-*hydroxy*-2-*methylquinoline*-3-*carboxylic acid*, m. p. 259° (decomp.) (from dimethylformamide), was obtained when the preceding carboxylic acid was reduced by zinc dust in acetic acid (Found: C, 48·9; H, 2·7; N, 5·1. $C_{11}H_7Cl_2NO_3$ requires C, 48·5; H, 2·6; N, 5·1%). It was decarboxylated on being heated at 250°, yielding 6,8-dichloro-4-hydroxyquinaldine (III), identified (m. p. 298° and infrared spectrum) by comparison with a specimen prepared essentially as described by Hughes and Lyons [2] who give m. p. 290°.

(*f*) *Ethyl* 6-*bromo*-8-*chloro*-1,4-*dihydro*-1-*hydroxy*-2-*methyl*-4-*oxoquinoline*-3-*carboxylate*, m. p. 193° (from ethanol; yield 55%) (Found: C, 43·6; H, 3·3; N, 3·8. $C_{13}H_{11}BrClNO_4$ requires C, 43·3; H, 3·1; N, 3·9%), and *ethyl* α-(5-*bromo*-2-*nitrobenzylidene*)*acetoacetate*, m. p. 106° (from ethanol) (Found: C, 45·7; H, 3·8; N, 3·9. $C_{13}H_{12}BrNO_5$ requires C, 45·6; H, 3·5; N, 4·1%), were obtained from 5-bromo-2-nitrobenzaldehyde and ethyl acetoacetate in ethereal hydrogen chloride. The quinolone was acetylated to the 1-*acetoxy-compound*, m. p. 122° (from ethanol) (Found: C, 45·0; H, 2·9; N, 3·8. $C_{15}H_{13}BrClNO_5$ requires C, 44·7; H, 3·2; N, 3·5%), which by hydrogenolysis over palladium–charcoal in ethanol gave ethyl 4-hydroxyquinaldine-3-carboxylate.

(*g*) 3-Acetyl-1,4-dihydro-1-hydroxy-2-methyl-4-oxoquinoline, m. p. and mixed m. p. 261°,[1] was formed in ethereal hydrogen bromide from *o*-nitrobenzaldehyde and acetylacetone (yield 60%) or from preformed 2-nitrobenzylideneacetylacetone (yield 80%). The derived 1-*acetoxy-compound*, m. p. 137° (from ethanol) (Found: C, 65·0; H, 4·6; N, 5·6. $C_{14}H_{13}NO_4$ requires C, 64·9; H, 5·0; N, 5·4%), upon hydrogenolysis afforded 3-*acetyl*-4-*hydroxyquinaldine*, m. p. 255° (from dimethylformamide) (Found: C, 72·0; H, 5·5; N, 7·3. $C_{12}H_{11}NO_2$ requires C, 71·6; H, 5·5; N, 7·0%), likewise obtained from 1-acetoxy-3-acetyl-6-chloro-1,4-dihydro-2-methyl-4-oxoquinoline.

Anthranils.—A solution of the nitrobenzaldehyde (0·01 mol.) and phenol (0·02 mol.) in anhydrous ether (*ca.* 30 ml.) was saturated with the hydrogen halide at room temperature and, after 24 hr., the precipitate of anthranil(s) was collected, any unchanged aldehyde being recovered from the mother-liquor. For reactions involving quinol (0·02 mol.) tetrahydrofuran was used as solvent (despite its interaction with hydrogen halide), volatile material was removed *in vacuo* after 24 hr., and the resultant solid was triturated with water.

3-p-*Hydroxyphenylanthranil*, m. p. 205° (from methanol), as the more soluble fraction was formed together with its 5-bromo-derivative (see below) in the approximate weight ratio of 1 : 3 from *o*-nitrobenzaldehyde and phenol in ethereal hydrogen bromide (Found: C, 74·1; H, 4·2; N, 6·8. $C_{13}H_9NO_2$ requires C, 73·9; H, 4·3; N, 6·7%).

5-*Chloro*-3-p-*hydroxyphenylanthranil*, m. p. and mixed m. p. 242° (from dimethylformamide),[6] was formed (*a*) almost quantitatively from *o*-nitrobenzaldehyde and phenol in ethereal hydrogen chloride, (*b*) in 50% yield (after allowance for recovered aldehyde) from 5-chloro-2-nitrobenzaldehyde and phenol in ethereal hydrogen bromide (Found: C, 63·2; H, 3·3; N, 5·9. Calc. for $C_{13}H_8ClNO_2$: C, 63·5; H, 3·3; N, 5·7%).

A warm solution of the anthranil (1 g.) in 10% aqueous sodium hydroxide (10 ml.) was treated portionwise with sodium dithionite (6 × 0·5 g.) until the initial orange-red colour had faded to pale yellow. Acidification with dilute acetic acid then gave 2-amino-5-chloro-4′-hydroxybenzophenone,[7] m. p. 177° (from methanol–water) (Found: C, 63·2; H, 4·3; N, 5·9. Calc. for $C_{13}H_{10}ClNO_2$: C, 63·0; H, 4·1; N, 5·7%). The *diacetyl derivative*, m. p. 137° (from ethanol–water) (Found: C, 61·5; H, 4·3; N, 4·3. $C_{17}H_{14}ClNO_4$ requires C, 61·5; H, 4·2; N, 4·2%), thereof was partially hydrolysed by 0·5N-sodium hydroxide at 100°, affording 2-*acetamido*-5-*chloro*-4′-*hydroxybenzophenone*, m. p. 174° (from ethanol–water) (Found: C, 62·3; H, 4·3; N, 5·0. $C_{15}H_{12}ClNO_3$ requires C, 62·2; H, 4·2; N, 4·8%). This phenol when oxidised by potassium permanganate (2% solution) gave *N*-acetyl-5-chloroanthranilic acid, identified by mixed m. p. 202° and infrared spectrum.

5-*Bromo*-3-p-*hydroxyphenylanthranil*, m. p. 243° (from dimethylformamide–water) was formed (yield 40% after allowance for recovered aldehyde) from 5-bromo-2-nitrobenzaldehyde and phenol in ethereal hydrogen bromide (Found: C, 53·4; H, 2·6; N, 5·1. $C_{13}H_8BrNO_2$ requires C, 53·8; H, 2·8; N, 4·8%).

5,7-*Dichloro*-3-p-*hydroxyphenylanthranil*, m. p. 251° (from ethanol), was obtained in almost quantitative yield from 5-chloro-2-nitrobenzaldehyde and phenol in ethereal hydrogen chloride (Found: C, 55·5; H, 2·8; N, 5·1. $C_{13}H_7Cl_2NO_2$ requires C, 55·7; H, 2·5; N, 5·0%).

When degraded, by the procedure described for the 5-chloro-analogue, *via* 2-*amino*-3,5-*dichloro*-4′-*hydroxybenzophenone*, m. p. 162° (from ethanol–water) (Found: C, 55·5; H, 3·3; N, 5·1. $C_{13}H_9Cl_2NO_2$ requires C, 55·4; H, 3·2; N, 5·1%), its ON-*diacetyl derivative*, m. p. 193° (from acetic acid) (Found: C, 56·1; H, 3·6; N, 3·7. $C_{17}H_{13}Cl_2NO_4$ requires C, 55·8; H, 3·6; N, 3·8%), and its N-*acetyl derivative*, m. p. 280° (from ethanol) (Found: C, 55·6; H, 3·5; N, 4·1. $C_{15}H_{11}Cl_2NO_3$ requires C, 55·6; H, 3·4; N, 4·3%), the anthranil gave *N*-acetyl-3,5-dichloroanthranilic acid, identified by m. p. and mixed m. p. 205° and by its infrared spectrum.

5-*Bromo*-7-*chloro*-3-p-*hydroxyphenylanthranil*, m. p. 241° (from dimethylformamide–water) (yield 94%), was obtained from 5-bromo-2-nitrobenzaldehyde and phenol in ethereal hydrogen chloride (Found: C, 48·1; H, 2·1; N, 4·5. $C_{13}H_7BrClNO_2$ requires C, 48·1; H, 2·2; N, 4·3%).

2-*Amino*-4′-*hydroxydiphenylmethane*, m. p. 117° (from ethanol), was formed from each of the foregoing mono- or di-halogenoanthranils by hydrogenolysis over palladium–charcoal (Found: C, 78·7; H, 6·8; N, 7·1. $C_{13}H_{13}NO$ requires C, 78·4; H, 6·5; N, 7·1%). When warmed in acetic anhydride it gave the *diacetyl derivative*, m. p. 175° (from ethanol) (Found: C, 72·1; H, 6·1; N, 5·2. $C_{17}H_{17}NO_3$ requires C, 72·1; H, 6·0; N, 4·9%).

3-(2,5-*Dihydroxyphenyl*)*anthranil*, m. p. 200° (from ethanol–water), was formed (yield 50%) from *o*-nitrobenzaldehyde, quinol, and hydrogen chloride (Found: C, 68·6; H, 4·1; N, 6·0. $C_{13}H_9NO_3$ requires C, 68·7; H, 4·0; N, 6·2%). It was oxidised by sodium dichromate in aqueous acetic acid at 100°, affording anthranil-3-carboxylic acid [10] which was recovered in chloroform and identified by m. p. and mixed m. p. 192° (from water), by its infrared spectrum, and by conversion with acetic anhydride into *N*-acetylanthranilic acid, m. p. and mixed m. p. 188°.

5-*Chloro*-3-(2,5-*dihydroxyphenyl*)*anthranil*, m. p. 254° (from methanol), was obtained (yield

[10] Arndt, Eistert, and Partale, *Ber.*, 1927, **60**, 1364.

60%) from 2-chloro-5-nitrobenzaldehyde, quinol, and either hydrogen chloride or hydrogen bromide (Found: C, 59·3; H, 2·9; N, 5·6. $C_{13}H_8ClNO_3$ requires C, 59·6; H, 3·1; N, 5·4%).

5-*Bromo*-3-(2,5-*dihydroxyphenyl*)*anthranil*, m. p. 260° (from methanol), was obtained (yield 70%) from 5-bromo-2-nitrobenzaldehyde, quinol, and either hydrogen chloride or hydrogen bromide (Found: C, 51·0; H, 2·8; N, 4·6. $C_{13}H_8BrNO_3$ requires C, 51·0; H, 2·6; N, 4·6%). It was also obtained (yield 29%), together with 3-(2,5-dihydroxyphenyl)anthranil (yield 33%) by fractionating in methanol the mixed anthranils formed from *o*-nitrobenzaldehyde, quinol, and hydrogen bromide.

Reactions with o-*Nitrosobenzoic Acid*.—This acid was allowed to react with hydrogen chloride in tetrahydrofuran for 24 hr. at 20°. Concentration and addition of ether caused precipitation of 5-chloroanthranilic acid as the hydrochloride, from which the amino-acid was recovered and identified by mixed m. p. and by its infrared spectrum.

5-Bromoanthranilic acid was similarly obtained and identified when hydrogen bromide was used as condensing agent.

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