ortho-*Hydroxylation of Phenols. Part IV.* Pyrogallols.*

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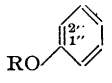
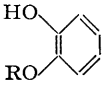
From phenol and its appropriate homologues, *via* 2-aryloxy-3 : 5-dinitrobenzophenones and the derived 2-2″-hydroxyaryloxy- and 2-(2″ : 6″-dihydroxyaryloxy)-3 : 5-dinitrobenzophenones, there are prepared pyrogallol, its 4-methyl, 5-methyl, 4 : 5-dimethyl, and 4 : 6-dimethyl derivatives.

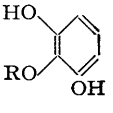
As was shown in Part III * 2-aryloxy-5-nitrobenzophenones (I*a*) may be hydroxylated in successive stages to (II*a*) and (III*a*), but interaction of piperidine with compounds of type (III*a*) causes rearrangement and cyclisation to fluorones instead of scission to pyrogallols. In the hope of securing conditions more favourable to scission, 2-aryloxy-



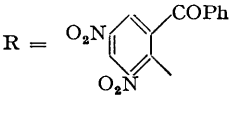
(I)
(I*a*)

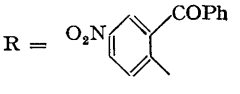


(II)
(II*a*)



(III)
(III*a*)





3 : 5-dinitrobenzophenones were examined and, with these compounds (I) and their hydroxylation products (II) and (III) as intermediates, the conversion of phenols into the corresponding pyrogallols has now been accomplished.

* Part III, *J.*, 1953, 269.

The greater reactivity of 2-chloro-3 : 5-dinitrobenzophenone over the 5-mononitro-compound enabled diaryl ethers of type (I) to be prepared by reaction with phenols in pyridine at ordinary temperature (cf. Borrows, Clayton, Hems, and Long, *J.*, 1949, S190). Ethers of more sensitive phenols, such as naphthols, and of polyhydric phenols are thereby made available for study (cf. Table 1). Hydroxylation of the dinitro-ethers proceeded

TABLE 1. 2-*Aryloxy*-3 : 5-*dinitrobenzophenones.*

No.	Subst.	M. p.	Formula	Found, % C	Found, % H	Required, % C	Required, % H
I	—	142°	$C_{19}H_{12}O_6N_2$	62·6	3·2	62·6	3·3
IV	3″-Me	159	$C_{20}H_{14}O_6N_2$	63·55	3·9	63·5	3·7
V	4″-Me	130	,,	63·8	3·5	,,	,,
VI	2″ : 5″-Me_2	146	$C_{21}H_{16}O_6N_2$	64·5	3·8	64·3	4·1
VII	3″ : 4″-Me_2	164	,,	64·5	4·3	,,	,,
VIII	3″ : 5″-Me_2	217	,,	64·5	4·2	,,	,,
II	2″-OH	160	$C_{19}H_{12}O_7N_2$	59·9	3·3	60·0	3·2
IX	3″-OH	160—163	,,	60·1	3·2	,,	,,
X	2″ : 3″-Benzo	155	$C_{23}H_{14}O_6N_2$	67·0	3·7	66·7	3·4
XI	3″ : 4″-Benzo	188	,,	66·9	3·0	,,	,,
XII	2″ : 3″-α-Naphtho †	248	$C_{27}H_{16}O_6N_2$	70·0	3·7	69·8	3·5

† From 1-phenanthrol.

essentially as described for the mononitro-ethers (Part II, *J.*, 1953, 265; Part III, *loc. cit.*) but with less allowable latitude in experimental conditions. The restriction is probably imposed by the greater sensitivity of the hydroxylated dinitro-compounds which, in general, are less easily handled and more prone to deterioration on storage. 2-2″-Hydroxyphenoxy-3 : 5-dinitrobenzophenone (II) was alternatively prepared by hydroxylating 2-phenoxy-3 : 5-dinitrobenzophenone (I) and by condensing catechol with 2-chloro-3 : 5-dinitrobenzophenone. It underwent scission when treated with piperidine at room temperature under a variety of conditions, and the products were identified as catechol and 3 : 5-dinitro-2-piperidinobenzophenone. 3 : 6-Dimethylcatechol was also obtained in good yield from 2-(2″-hydroxy-3″ : 6″-dimethylphenoxy)-3 : 5-dinitrobenzophenone (XV) which was prepared *via* the ether (VI) from 2 : 5-dimethylphenol. Scission of the other hydroxyaryloxy-3 : 5-dinitrobenzophenones, listed in Table 2, was not attempted but compounds (XIII) and (XIV) require further comment. Despite their identical m. p.s and the fact that this value is scarcely, if at all, depressed by admixture of the samples, the compounds are quite distinct as is shown by the results of renewed hydroxylation (see Table 3). None the less on methylation by diazomethane in ether they both yielded the same product, namely 2-(2″-methoxy-4″-methylphenoxy)-3 : 5-dinitrobenzophenone, of which the structure was proved in each case by scission with piperidine to 4-hydroxy-3-methoxytoluene. Both compounds are accordingly derived from 3 : 4-dihydroxytoluene but in course of methylation (XIII) undergoes rearrangement to (XIV). Although similar rearrangement has previously been observed under alkaline conditions in the mononitro-series, this is the first instance of its occurrence during methylation by diazomethane.

TABLE 2. 2-2″-*Hydroxyaryloxy*-3 : 5-*dinitrobenzophenones.*

No.	Subst.	Source	M. p.	Formula	Found, % C	Found, % H	Required, % C	Required, % H
II	—	I	160°		see Table I			
XIII	5″-Me	IV	139	$C_{20}H_{14}O_7N_2$	60·85	3·6	60·9	3·55
XIV	4″-Me	V	139	,,	60·95	3·6	,,	,,
XV	3″ : 6″-Me_2	VI	171	$C_{21}H_{16}O_7N_2$	61·8	3·9	61·8	3·9
XVI	4″ : 5″-Me_2	VII	175	,,	62·0	4·1	,,	,,
XVII	3″ : 5″-Me_2	VIII	183 *	,,	61·6	4·0	,,	,,

It recalls the similar methylation of 2-acylalizarin to 1-acylalizarin 2-methyl ether (Perkin and Storey, *J.*, 1928, 229).

Renewed hydroxylation of the compounds of Table 2 was successful in all except (XV) which lacks the requisite free *o*-position. The solid obtained from (XVII) could not be crystallised but subsequent scission showed that it was substantially the expected product.

Scission of the dihydroxy-compounds (Table 3) was much more rapid than in the mononitro-series and could be effected at room temperature even in presence of diluents. Tests showed that scission was more reliably achieved by phenylhydrazine than by piperidine—with which fluorone formation was again observed—and the former reagent was accordingly

TABLE 3. 2-(2'' : 6''-*Dihydroxyaryloxy*)-3 : 5-*dinitrobenzophenones.*

No.	Subst.	Source	M. p.	Formula	Found, % C	Found, % H	Required, % C	Required, % H
III	—	II	148° *	$C_{19}H_{12}O_8N_2$	57·6	3·3	57·6	3·0
XVIII	3''-Me	XIII	206 *	$C_{20}H_{14}O_8N_2$	58·5	3·4	58·5	3·4
XIX	4''-Me	XIV	164 *	,,	58·7	3·6	,,	,,
XX	3'' : 4''-Me_2	XVI	203 *	$C_{21}H_{16}O_8N_2$	59·7	3·7	59·4	3·8

* Decomp.

adopted. Thereby (III) was smoothly converted into pyrogallol, with 5 : 7-dinitro-1 : 3-diphenylindazole as an easily separable by-product, and by similar means the two monomethyl and the two dimethyl homologues of pyrogallol were prepared.

EXPERIMENTAL

(Petroleum as solvent refers to light petroleum of b. p. 60—80°).

2-*Aryloxy*-3 : 5-*dinitrobenzophenones* (Table 1).—The phenol in slight excess was added to a solution of 2-chloro-3 : 5-dinitrobenzophenone in pure dry pyridine and, after 15 hr., the whole was poured into dilute acid. The resultant solid compounds (I), (IV), (V), (VII), and (VIII) were crystallised from methanol–benzene; (VI) was crystallised from benzene–petroleum; (X) and (XI) from acetic acid; and (XII) from xylene. Compounds (II) and (IX) were crystallised from methanol and were best prepared by using a 6 molar excess of the dihydric phenol in order to minimise formation of di-ethers. *Catechol bis-*(2-*benzoyl*-4 : 6-*dinitrophenyl*) *ether*, m. p. 160° (from acetic acid) (Found : C, 59·3; H, 3·0. $C_{32}H_{18}O_{12}N_4$ requires C, 59·1; H, 2·8%), and *resorcinol bis*(2-*benzoyl*-4 : 6-*dinitrophenyl*) *ether*, m. p. 115° (from acetic acid) (Found, after fusion *in vacuo* : C, 58·9; H, 2·7%), were readily formed when 0·5 molar proportions of the phenols were used.

2-2''-*Hydroxyaryloxy*-3 : 5-*dinitrobenzophenones* (Table 2).—The following is typical : Powdered 3 : 5-dinitro-2-phenoxybenzophenone (0·1 g.) was dissolved in warm concentrated sulphuric acid (0·5 c.c.), and after 30 min. acetic acid (2·5 c.c.) was added. The red solution was allowed to cool and was then titrated with a solution of 30% hydrogen peroxide in acetic acid (1 : 2 by vol.) until a slight excess of the oxidising agent was present. After 15—30 min., when the colour of the solution had faded to amber and in some cases the product had crystallised, the whole was stirred into crushed ice, and the resultant solid crystallised from methanol. Compounds (XV), (XVI), and (XVII) were crystallised from methanol, ethanol, and aqueous ethanol, respectively; compounds (XIII) and (XIV) from benzene–petroleum and, as frequently observed with these solvents, the crystals retained solvent which was removed at 125° *in vacuo*. On one occasion compound (XIII) was obtained with m. p. 159° (from benzene–petroleum) changing to m. p. 146° when kept *in vacuo* at 125° (Found : C, 61·05; H, 3·8%).

2-(2'' : 6''-*Dihydroxyaryloxy*)-3 : 5-*dinitrobenzophenones* (Table 3).—Acetic acid (3·5 c.c.) was added to the monohydroxy-compound (0·1 g.) in concentrated sulphuric acid (0·5 c.c.), affording dark red-brown solutions from (II) and (XIV), and dark green solutions from (XIII), (XVI), and (XVII). After titration with a slight excess of the hydrogen peroxide–acetic acid solution, the colour changed to amber within 10 min., and the whole was at once added to ice. The products crystallised with difficulty, deteriorating in hot solution and retaining (hydrocarbon) solvents in the crystals. For analysis (III) was crystallised from acetic acid–petroleum; (XVIII) from chloroform; (XIX) from benzene, with subsequent heating at 140° *in vacuo*; and (XX) from methanol. Hydroxylation of (XVII) (0·1 g.) was best effected by using increased quantities of sulphuric (3 c.c.) and acetic (10 c.c.) acids, but the product, although a solid, could not be crystallised and was directly used for scission to 4 : 6-dimethylpyrogallol.

Scissions.—With piperidine. 3 : 5-Dinitro-2-phenoxybenzophenone (I) and piperidine reacted vigorously alone and, more slowly, in solution in cold benzene even in presence of acetic acid equivalent to the quantity of amine used. After several hours, in all three cases phenol was recovered in alkali from a solution of the products in benzene and was identified as tribromophenol. The residual benzene solution, when acid-washed, dried and concentrated, and the concentrate treated with petroleum, afforded 3 : 5-*dinitro*-2-*piperidinobenzophenone*

as orange plates, m. p. 125° (from ethanol), also prepared from piperidine and 2-chloro-3 : 5-dinitrobenzophenone (Found : C, 60·9; H, 5·0. $C_{18}H_{17}O_5N_3$ requires C, 60·8; H, 4·8%). In corresponding experiments with (II) in place of (I) catechol was isolated, being recovered in ether after saturation of the acidified alkaline extract with ammonium sulphate, and was purified by sublimation.

When treated (48 hr.) with diazomethane in ether, compound (XIV) afforded 2-(2''-*methoxy*-4''-*methylphenoxy*)-3 : 5-*dinitrobenzophenone*, m. p. 186°, from benzene–petroleum (Found : C, 62·0; H, 4·0. $C_{21}H_{16}O_7N_2$ requires C, 61·8; H, 3·9%), and the same compound, m. p. and mixed m. p. 186—187°, was likewise produced from (XIII). In separate experiments a sample of the product (1 mol.) from each source was suspended in benzene, treated with piperidine (3 mol.) and, after 15 hr., the resultant solution was extracted with aqueous sodium hydroxide from which by acidification, saturation with ammonium sulphate, and recovery in ether, 4-hydroxy-3-methoxytoluene was obtained as an oil. In each case the scission product was identified as the picrate, (micro-) m. p. 104° (cf. Part I; *J.*, 1950, 55), and benzoate, m. p. 72° (Cosgrove and Waters, *J.*, 1949, 3189, give m. p. 73°) (the picrate and benzoate of 3-hydroxy-4-methoxytoluene have m. p.s 87·5° and 81°, respectively).

A solution of (III) (1 mol.) in benzene and piperidine (4 mol.) was extracted after 24 hr. with aqueous sodium hydroxide which, on acidification, afforded 4-*hydroxy*-5 : 7-*dinitro*-9-*phenylfluorone* as black crystals, m. p. (decomp.) 335° (from anisole : they were ground under methanol before analysis) (Found : C, 60·45; H, 2·9. $C_{19}H_{10}O_7N_2$ requires C, 60·3; H, 2·65%). When a large excess of piperidine was used neither the fluorone nor pyrogallol could be obtained from the alkaline extract, but the residual benzene solution afforded 3 : 5-dinitro-2-piperidinobenzophenone.

With hydroxylamine. A solution of (III) (1 mol.) and hydroxylamine (1 mol.; from the hydrochloride and sodium acetate) in methanol was filtered after 3 hr. from the crystalline precipitate of 5 : 7-dinitro-3-phenylbenz*iso*oxazole (m. p. 244°, from benzene, undepressed by admixture with a sample prepared as described by Meisenheimer, Zimmerman, and Kummer, *Annalen*, 1925, **446**, 205), and the filtrate was diluted with ether. The ethereal solution, successively washed with aqueous sodium carbonate, dilute acid, and water, was dried and concentrated. Sublimation of the residue at 20 mm. afforded pyrogallol, m. p. 126° raised to 128—130° by admixture with an authentic sample. The yield was poor.

With phenylhydrazine. A solution of the compound (1 mol.) and phenylhydrazine (5 mol.) in benzene was kept for 15 hr. It was then extracted with dilute sodium hydroxide, and the aqueous layer immediately run into dilute sulphuric acid. The acid solution was saturated with ammonium sulphate and exhausted with ether. The material recovered from the dried ethereal solution was sublimed at 20 mm. and the phenolic sublimate was further purified as required. The residual benzene solution contained 5 : 7-dinitro-1 : 3-diphenylindazole which, after the excess of phenylhydrazine was washed out by aqueous acetic acid, was recovered as plates, of m. p. 218°, from ethanol, m. p. undepressed by admixture with an authentic sample (Borsche and Scriba, *Annalen*, 1939, **540**, 83) (Found : C, 63·3; H, 3·5. Calc. for $C_{19}H_{12}O_4N_4$: C, 63·3; H, 3·3%). The following were thus prepared : Catechol, m. p. and mixed m. p. 105°, from benzene–petroleum; from (II). 3 : 6-Dimethylcatechol, needles (from benzene–petroleum), m. p. 102° undepressed with a sample prepared as in Part II (*loc. cit.*); from (XV).

Pyrogallol, m. p. and mixed m. p. 132°, from benzene; from (III).

4-Methylpyrogallol, m. p. 142°, from benzene–petroleum; from (XVIII) (Found : C, 60·1; H, 5·8. Calc. for $C_7H_8O_3$: C, 60·0; H, 5·7%). Majima and Okasaki (*Ber.*, 1916, **49**, 1492) give m. p. 140—141°.

5-Methylpyrogallol, m. p. 120°, from benzene; from (XIX) (Found : C, 60·2; H, 5·9%). Recorded m. p.s range from 119 to 129°.

4 : 5-*Dimethylpyrogallol*, m. p. 148°, from benzene; from (XX) (Found : C, 62·6; H, 6·6. $C_8H_{10}O_3$ requires C, 62·3; H, 6·5%).

4 : 6-Dimethylpyrogallol, m. p. and mixed m. p. 122—123° (Part III; *loc. cit.*); from the solid hydroxylation product of (XVII).

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