CLXVIII.—*A New Method for the Preparation of 2 : 4-Dihydroxy- and 2 : 4 : 4'-Trihydroxy-benzophenone, and some Observations relating to the Hoesch Reaction.*

By HENRY STEPHEN.

IN Hoesch's method (*Ber.*, 1915, **48**, 1122) for the preparation of aromatic hydroxy-ketones by condensing phenolic compounds with nitriles in the presence of hydrogen chloride, the formation of an imino-chloride, $CRCl\colon NH$, is assumed, and this compound condenses with the phenolic compound to yield the ketimine, $CRR'\colon NH$. The latter yields the corresponding ketone on hydrolysis. Cyanogen bromide is exceptional in its behaviour towards hydrogen chloride (compare Karrer, *Helv. Chim. Acta*, 1919, **2**, 89). References to the formation of additive compounds (imino-haloids) of nitriles and hydrogen haloids are given in the literature (Gauthier, *Annalen*, 1869, **150**, 187; Michael and Wing, *Amer. Chem. J.*, 1885, **7**, 71), but the most definite evidence of the formation of such additive compounds was obtained by Tröger and Lüning (*J. pr. Chem.*, 1904, [ii], **69**, 347), who obtained chloroacetimide chloride, $CH_2Cl\cdot CCl\colon NH$, from chloroacetonitrile and hydrogen chloride. The author has prepared this compound, and found that, on mixing it with the theoretical amount of resorcinol and warming on the water-bath at 50—60°, hydrogen chloride was evolved, ω-chlororesacetophenone (needles, m. p. 131°) being subsequently isolated from the product. Sonn (*Ber.*, 1917, **50**, 1262) has condensed chloroacetonitrile with resorcinol according to Hoesch's method, and obtained the same substance. The mechanism of the reaction is therefore explained as follows, according to the above experiment:

$$C_6H_4(OH)_2 + CH_2Cl\cdot CCl\colon NH \xrightarrow{-HCl} \underset{\text{(I.)}}{C_6H_3(OH)_2\cdot C(\colon NH)\cdot CH_2Cl},$$

the ketimine (I) yielding the ketone on hydrolysis.

Further evidence of the mechanism of the Hoesch reaction is afforded by the fact that certain *N*-substituted imino-chlorides, for example, benzanilideiminochloride, $CPhCl\colon NPh$, react on warming with resorcinol, yielding the anils of the corresponding hydroxy-ketones. Thus, in the case of benzanilideiminochloride, the anil

(II) of 2:4-dihydroxybenzophenone is obtained as follows, and, on hydrolysis, yields the ketone:

$$C_6H_4(OH)_2 + CPhCl{:}NPh \xrightarrow{-HCl} \underset{\text{(II.)}}{C_6H_3(OH)_2{\cdot}CPh{:}NPh}.$$

In a similar way, 2:4:4′-trihydroxybenzophenone,

$$OH{\cdot}C_6H_4{\cdot}CO{\cdot}C_6H_3(OH)_2$$

(III), was obtained from *p*-ethylcarbonatobenzanilideiminochloride (Sonn and Müller, *Ber.*, 1919, **52**, 1927).

An attempt to prepare 2:4-dihydroxyphenyl styryl ketone* by condensing cinnamanilideiminochloride with resorcinol was unsuccessful.

It may be mentioned that cinnamanilideiminochloride, prepared according to Sonn and Müller's method (*loc. cit.*), is a solid crystallising from toluene in clusters of needles melting at 30°, and not a red, viscous mass, as described by these authors, although if heated for some time on the water-bath the crystals change into a red mass.

The failure to prepare 2:4-dihydroxyphenyl styryl ketone is parallel to that of Fischer and Nouri (*Ber.*, 1917, **50**, 693), who attempted to prepare 2:4:6-trihydroxyphenyl styryl ketone from phloroglucinol and cinnamonitrile by Hoesch's method, and obtained instead 5:7-dihydroxy-4-phenyl-3:4-dihydro-1:2-benzopyrone. This anomalous behaviour is due, apparently, to the unsaturated nature of the nitrile, since phloretonitrile (*β*-*p*-hydroxyphenylpropionitrile) condenses in the usual way with resorcinol or phloroglucinol.

In carrying out the condensations of the *N*-substituted iminochlorides with resorcinol, certain observations have led the author to believe that an imino-ether is the first product of the reaction, which then undergoes isomeric change, resulting in a shift of the group ·CPh:NPh into the nucleus in the ortho- and para-positions with respect to the hydroxyl groups. Thus, in the case of benzanilideiminochloride, the preliminary reaction may be represented

---

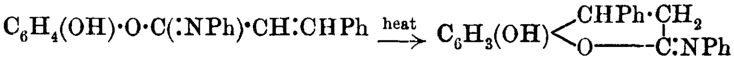
* This ketone cannot be prepared by condensing resorcinol and cinnamonitrile according to Hoesch's method for reasons which are given later. Bargellini and Marantonio (*Atti R. Accad. Lincei*, 1908, [v], **17**, ii, 119) state that the same ketone can be prepared by fusing cinnamic acid and resorcinol with anhydrous zinc chloride. This experiment was repeated in order to obtain a specimen of the ketone for purposes of comparison, and the details are so simple that no difficulty would be anticipated. After many attempts had been made, the method was abandoned, no trace of ketone being obtained, the chief result being the formation of a red-coloured substance the investigation of which was not pursued further, and the conclusion was drawn that the statement of the above authors was incorrect.

as follows, the imino-ether (IV) undergoing subsequent change to yield the anil (II):

$$C_6H_4(OH)_2 + CPhCl\!:\!NPh \xrightarrow{-HCl} \underset{\text{(IV.)}}{C_6H_3(OH)\cdot O\cdot CPh\!:\!NPh}.$$

The evidence in favour of this isomeric change depends on the observation that the best yield of the anil (II) was obtained by first warming the mixture of the imino-chloride and resorcinol on the water-bath until the evolution of hydrogen chloride ceased, and subsequently heating in an oil-bath at 150°. Several instances of isomeric change of acyl derivatives of phenols involving a migration of the acyl group into the nucleus are also known to take place on heating. The preliminary warming of the above mixture on the water-bath resulted in the formation of an oily product, which was found to be easily hydrolysed into benzanilide and resorcinol on boiling for a short time with dilute hydrochloric acid; this would be the behaviour expected of the imino-ether.

A similar observation was made in experiments with cinnamanilideiminochloride and resorcinol, and it is probable that the imino-ether (V) is first formed on the water-bath, but, on heating at a higher temperature in an oil-bath, this undergoes internal condensation, and not the above isomeric change, yielding the anil of 7-hydroxy-4-phenyl-3:4-dihydro-1:2-benzopyrone (VI):



$$C_6H_4(OH)\cdot O\cdot C(\!:\!NPh)\cdot CH\!:\!CHPh \xrightarrow{\text{heat}} C_6H_3(OH)\!<\!\begin{array}{l}CHPh\cdot CH_2\\ O\text{———}C\!:\!NPh\end{array}$$

(V.) (VI.)

This reaction is thus analogous to the formation of the benzopyrone investigated by Fischer and Nouri (*loc. cit.*). The imino-ether (V) was obtained as an oily product, which was easily hydrolysed to cinnamanilide and resorcinol on boiling for a few minutes with dilute hydrochloric acid or by prolonged boiling with water. The formation of the anil (VI) still remains in doubt, and is reserved for further investigation.

EXPERIMENTAL.

2:4-*Dihydroxybenzophenone* (*Benzoresorcinol*).

The benzanilideiminochloride used in this experiment was prepared from benzanilide which had been carefully purified. The method adopted was the same as that due to Wallach (*Annalen*, 1877, **184**, 86), and the product was purified by distillation under diminished pressure. Attempts were made to replace the phosphorus pentachloride as used in Wallach's method by thionyl chloride, but without success.

Three grams (1 mol.) of the imino-chloride were mixed with 2 grams (1 mol.) of resorcinol, and then warmed on the water-bath at 50°; when the evolution of hydrogen chloride had ceased, the mixture was transferred to an oil-bath and heated for ten minutes at 150°. Longer heating caused much decomposition, the product becoming darker in colour. The red-coloured mass was then boiled with water to remove any unchanged resorcinol, and the aqueous solution decanted from the viscid, red oil. This operation was repeated several times, and the oil allowed to remain in the refrigerator overnight. It showed no tendency to crystallise, being very readily soluble in most of the usual solvents. After several attempts, a small quantity of a bright yellow, crystalline compound separated from ethyl acetate, which melted and decomposed at 228—230°. There was, unfortunately, insufficient for an analysis.

Hydrolysis of the Anilide of 2:4-*Dihydroxybenzophenone.*

The most successful method of hydrolysis consisted in boiling the oil with about 25 per cent. hydrochloric acid. The oil was first treated with 50 c.c. of hydrochloric acid, boiled for fifteen minutes, and the yellow solution decanted and filtered from the tarry matter. This operation was repeated several times, the accumulated filtrates were boiled with animal charcoal, and, on filtering, a clear solution was obtained, from which long needles of 2:4-dihydroxybenzophenone separated. These melted at 144°, and were identical with a sample of the same substance prepared by condensing benzonitrile with resorcinol according to the method used by Hoesch, who prepared the substance in that way.

A more rapid method of hydrolysis, but one which leads to difficulty in the final stage of purification of the product, consists in heating the oil with sufficient dilute alcohol to dissolve it, and then passing in hydrogen chloride until the solvent is nearly saturated. The mixture was boiled for a whole day under a reflux condenser, and then filtered. Some tarry matter passed into the filtrate, owing to the alcohol present, and this causes difficulty in the purification of the ketone after evaporation of the alcohol, but by recrystallising the product several times from hot water and repeated treatment with animal charcoal, a pure sample of 2:4-dihydroxybenzophenone was obtained.

2:4:4′-*Trihydroxybenzophenone* (III).

The starting material for the experiment was *p*-ethylcarbonatobenzoic acid, which was prepared according to Fischer and

Freudenberg's method (*Annalen*, 1910, **372**, 36), by shaking 30 grams of *p*-hydroxybenzoic acid with 30 grams of ethyl chloroformate and 450 c.c. of *N*-sodium hydroxide. It crystallised from acetone in needles melting at 156°.

The acid chloride was prepared by heating 25 grams of the acid with 24 grams of phosphorus pentachloride. After removing the phosphoryl chloride, the acid chloride distilled at 170°/12 mm.

It was then converted into *p*-ethylcarbonatobenzanilide by dissolving 20 grams in dry benzene and gradually adding 17 grams (2 mols.) of aniline while shaking. A white solid, consisting of a mixture of aniline hydrochloride and *p*-ethylcarbonatobenzanilide, separated, and, after allowing to remain overnight, the precipitate was collected and triturated with very dilute hydrochloric acid to remove aniline hydrochloride. It was then collected, washed with water, then with dilute sodium hydrogen carbonate solution to remove any acid present, and again with water, and then dried.

Preparation of the Imino-chloride.

Five grams (1 mol.) of *p*-ethylcarbonatobenzanilide were suspended in dry toluene, 3·7 grams (1 mol.) of powdered phosphorus pentachloride added, and the mixture was warmed gently on the water-bath for fifteen minutes, when a clear solution was obtained. The phosphoryl chloride and toluene were then distilled off under diminished pressure, and the imino-chloride remained as a brown, crystalline mass. This was not purified, as it easily decomposes in air, but it melted at about 80°.

Condensation of Resorcinol with the Imino-chloride.

To the imino-chloride in the distillation flask, 2·5 grams (1 mol.) of resorcinol were added, and the mixture was warmed gently on the steam-bath. A reaction soon started, hydrogen chloride being evolved, and the mass became darker in colour. After heating for twenty minutes, the residue was dissolved in alcohol, about 2 c.c. of hydrochloric acid were added, and the mixture was boiled for several hours in order to hydrolyse the ethylcarbonato-group and the imino-group. The alcohol was then distilled off under diminished pressure, and the residue crystallised from hot water in pale yellow needles melting at 200°. It gave a purple coloration with ferric chloride in alcoholic solution, and was found to be 2:4:4′-trihydroxybenzophenone (Komarowski and Kostanecki, *Ber.*, 1894, **27**, 1999, give the melting point as 200—201°).

The author desires to express his thanks to Miss L. Higginbotham and Mr. W. K. Slater for assistance with certain parts of the experimental work.

THE CHEMICAL DEPARTMENT,
THE UNIVERSITY,
MANCHESTER.

[*Received, October* 14*th*, 1920.]