125. *The Reimer–Tiemann Reaction.*

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In an attempt to discover the mechanism of the Reimer–Tiemann reaction it seemed to us that the first step was to explain why such large amounts of unchanged phenol may be recovered in the isolation of the small yields of aldehyde afforded by this process. A possible cause of this was the non-homogeneity of the reaction mixture, and experiments were first made in which trichloroacetic acid was substituted for chloroform. A solution of phenol and trichloroacetic acid in aqueous potassium hydroxide boiled violently when cautiously heated, and only a small amount of free chloroform could be detected. Aldehydes were obtained from phenol, *o*-, *m*-, and *p*-cresols, -chlorophenols, and -hydroxybenzoic acids and *m*-nitrophenol, but the yields were no improvement on those afforded by the ordinary chloroform process, and large amounts of the phenols were recovered.

Potassium oxalate and tri-*p*-chlorophenyl orthoformate were isolated as by-products in the experiments with *p*-chlorophenol, and traces of di(chlorosalicylaldehyde) were indicated.

It then occurred to us that an intermediate such as hydroxybenzal chloride might lead to the formation of an acetal:

$$HO{\cdot}C_6H_4{\cdot}CHCl_2 + 2KOPh \longrightarrow HO{\cdot}C_6H_4{\cdot}CH(OPh)_2 + 2KCl.$$

In this way two-thirds of the phenol would be recovered unchanged when the product was acidified and steam-distilled.

Attempts to prepare *o*-hydroxybenzal chloride by the hydrolysis of its methyl ether and carbethoxy-derivative with hydrogen chloride resulted in resinification and decomposition at the high temperature required (230—240°). However, *o*-ethylcarbonatobenzal chloride was prepared from carbethoxysalicylaldehyde, and by condensation with sodium phenoxide gave carbethoxysalicylaldehyde diphenylacetal. Salicylaldehyde diphenylacetal was obtained from this, by alkaline hydrolysis, as a thick oil which resinified rapidly on vacuum distillation and was hydrolysed by acids and even by sodium bicarbonate.

Evidence was obtained that such an acetal is formed in the Reimer–Tiemann reaction and in the trichloroacetic acid process. *p*-Chlorophenol was used to avoid complication due to the formation of isomeric aldehydes, and the product, after extraction of tri-*p*-chlorophenyl orthoformate and di(chlorosalicylaldehyde), was treated in three ways: All free chlorosalicylaldehyde was removed by (1) shaking with sodium phenylhydrazine-*p*-sulphonate solution or (2) addition of excess of methylmagnesium iodide, but more chlorosalicylaldehyde was isolated from both products after boiling with dilute acid. (3) Methylation with excess of methyl sulphate and extraction of the alkaline product with ether gave an oil which yielded *p*-chlorophenol on boiling with dilute acid.

It is concluded that the Reimer–Tiemann reaction involves the stages:

$$C_6H_5{\cdot}OK + CHCl_3 + KOH \longrightarrow KCl + KO{\cdot}C_6H_4{\cdot}CHCl_2 + H_2O \quad . \quad . \quad (A)$$

$$KO{\cdot}C_6H_4{\cdot}CHCl_2 + 2KO{\cdot}C_6H_5 \longrightarrow KO{\cdot}C_6H_4{\cdot}CH(O{\cdot}C_6H_5)_2 + 2KCl \quad . \quad . \quad (B)$$

$$KO{\cdot}C_6H_4{\cdot}CHCl_2 + 2KO{\cdot}C_6H_5 + 2KOH \longrightarrow KO{\cdot}C_6H_4{\cdot}CH(C_6H_4{\cdot}OK)_2 + 2KCl + 2H_2O \quad (C)$$

$$3C_6H_5{\cdot}OK + CHCl_3 \longrightarrow CH(O{\cdot}C_6H_5)_3 + 3KCl \quad . \quad . \quad . \quad . \quad (D)$$

The suggestion that the resinous by-product (stage C) is a triphenylmethane derivative is not new, but is supported by the determination of hydroxyl in the resins obtained from various phenols by the trichloroacetic acid process. The values obtained were in fair agreement with those calculated for the corresponding trihydroxytriphenylmethane derivatives, in view of the impossibility of purifying the resins. The formation of a benzal chloride derivative as intermediate is further supported by the fact that benzal chloride itself gave a large amount of a very similar resin when heated with phenol in potassium hydroxide solution, and the percentage of hydroxyl was found to be very near that required for dihydroxytriphenylmethane. *o*-Ethylcarbonatobenzal chloride, similarly treated, also gave a resin, but none was obtained by boiling salicylaldehyde with phenol in potassium hydroxide solution.

EXPERIMENTAL.

The Reaction of Phenol with Trichloroacetic Acid in Potassium Hydroxide Solution.—Preliminary expts. showed that the max. yields of aldehyde could be obtained when phenols were heated with a solution of trichloroacetic acid in twice the theo. amount of 10*N*-KOH or NaOH calc. from the equation $C_6H_5{\cdot}OH + CCl_3{\cdot}CO_2H + 5KOH \longrightarrow HO{\cdot}C_6H_4{\cdot}CHO + 3KCl + K_2CO_3 + 3H_2O$. No advantage was found in using more than a slight excess of trichloroacetic acid.

To a solution of the phenol (0·1 mol.) in H_2O (70 c.c.) containing KOH (1·0 mol.), trichloroacetic acid (0·125 mol.) in H_2O (20 c.c.) was added. The mixture was cautiously heated and, when the violent boiling ceased (few min.), refluxed for 1 hr. The temp. attained 112° and very little $CHCl_3$ was detected. The product was made just acid with dil. H_2SO_4, steam-distilled, and extracted with Et_2O. Half the extract was dried and evaporated to give the yield of aldehyde + recovered phenol; the other half was evaporated and dissolved in 20% AcOH aq., and the aldehyde estimated by pptn. with excess of *p*-nitrophenylhydrazine in 20% AcOH aq. The accuracy of this method was tested on pure specimens of salicylaldehyde, 5-chloro-2-hydroxy-, 3-chloro-2-hydroxy-, 2-chloro-4-hydroxy-, 2-hydroxy-5-methyl-, and 4-hydroxy-2-methyl-benzaldehyde and gave results ranging from 94·9 to 103·2%. Non-volatile aldehydes were extracted from the residual liquid after it had been filtered from resinous products, which were also weighed after being dried in ethereal solution. No separation was effected of the isomeric aldehydes from *o*- and *m*-hydroxybenzoic acids and *m*-nitrophenol. *o*- and *p*-Nitrophenols yielded no aldehyde.

The ketonic compounds described by Auwers and Keil (*Ber.*, 1902, **35**, 4207) were isolated in 1·4% yield by steam-distillation of the alkaline products from *o*- and *p*-cresols. The results are tabulated below.

	2-Aldehyde, %.		4-Aldehyde, %.		Recovered phenol, %.		Resin, %.	
	Expt. 1.	Expt. 2.	Expt. 1.	Expt. 2.	Expt. 1.	Expt. 2.	Expt. 1.	Expt. 2.
Phenol	10·5	10·2	7·9	8·2	75·1	74·5	3·4	4·3
o-Cresol	1·8	2·1	8·5	7·5	31·8	30·5	53·2	52·0
m- „	15·8	16·5	13·2	12·2	58·3	59·4	5·7	6·4
p- „	21·8	22·3	—	—	51·4	50·7	21·5	20·4
o-Chlorophenol	15·7	14·6	7·2	6·5	59·1	60·0	12·7	11·8
m- „	16·7	16·6	13·8	13·0	57·0	56·0	9·6	9·7
p- „	20·2	21·3	—	—	68·0	66·8	5·2	6·0
o-Hydroxybenzoic acid ...	16·8	17·0	—	—	79·5	78·5	—	—
m- „ „ ...	7·7	7·2	—	—	87·2	86·1	—	—
p- „ „ ...	14·7	14·0	—	—	80·1	82·1	—	—
m-Nitrophenol	3·4	2·8	—	—	72·3	71·0	20·0	22·0

Expts. with *p*-chlorophenol on a larger scale (1 mol.) yielded also potassium oxalate (2·35 g., filtered from the cooled reaction mixture) and tri-*p*-chlorophenyl orthoformate (12·3 g., extracted from the filtrate with $CHCl_3$). The latter product, recryst. from EtOH, was hydrolysed with dil. H_2SO_4 and found to contain 2·8% of chlorosalicylaldehyde. This was no doubt formed by the hydrolysis of a small quantity of di(chlorosalicylaldehyde), since disalicylaldehyde (m. p. 128°) was obtained in small amount by the steam-distillation of the alkaline product of the reaction of phenol and trichloroacetic acid with KOH. The tri-*p*-chlorophenyl orthoformate was further purified by recrystn. three times from 70% AcOH aq.; it then melted at 104° and gave on hydrolysis formic acid (11·4%; theo., 11·6) and *p*-chlorophenol (96·2%; theo., 97·5), estimated as the dibromo-derivative, m. p. 90° (benzoyl derivative, m. p. 93°).

Preparation and Hydrolysis of o-*Methoxybenzal Chloride and* o-*Ethylcarbonatobenzal Chloride.*—Salicylaldehyde methyl ether was added slowly with cooling to the theo. amount of PCl_5, and the product rapidly distilled at 35 mm., *o*-methoxybenzal chloride being obtained (yield, 84%), b. p. 136—142°/35 mm. When boiled with H_2O for 10 min., 1·2905 g. gave 13·6 c.c. of *N*-acid (theo., 13·5), 36·5% of Cl (theo., 37·2), and 70·3% of salicylaldehyde methyl ether (as *p*-nitrophenylhydrazone) (theo., 71·2).

Carbethoxysalicylaldehyde, obtained from 46 g. of ethyl chlorocarbonate and 50 g. of salicylaldehyde in 300 c.c. of *iso*propyl ether containing 84 g. of dry powdered K_2CO_3 after 24 hr. by distillation of the filtered liquid under reduced press., was a thick oil, b. p. 168—170°/30 mm. (yield, 29—36% in four expts.). 1·45 G. gave 60·4% of salicylaldehyde estimated as *p*-nitrophenylhydrazone (theo., 62·9). The phenylhydrazone had m. p. 101°, as given by Cajar (*Ber.*, 1898, **31**, 2804). Treatment with the theo. amount of PCl_5 and distillation under reduced press. gave a 75—80% yield of a thick oil, b. p. 178—182°/55 mm., d 1·300, n_D 1·525. It was completely hydrolysed to salicylaldehyde by boiling with H_2O for 1 hr. (1·163 g. gave 18·7 c.c. of *N*/2-HCl. Theo. for $EtO_2C{\cdot}O{\cdot}C_6H_4{\cdot}CHCl_2$, 18·7), and was slowly hydrolysed by cold KOH aq.

Preparation of Carbethoxysalicylaldehyde Diphenylacetal and Salicylaldehyde Diphenylacetal.—*o*-Ethylcarbonatobenzal chloride (49·8 g.) was slowly added to PhOH (37·6 g.) in abs. EtOH (400 c.c.) containing Na (9·2 g.), the pptd. NaCl (93% of theo. amount) removed, most of the

EtOH evaporated under reduced press., and $\mathrm{Et_2O}$ added to the remainder. Filtration and evaporation of the $\mathrm{Et_2O}$ left 69·6 g. (96%) of a green oil which turned brown on keeping, but when the ethereal solution was twice shaken with NaOH and evaporated, a colourless oil free from aldehyde was obtained (0·955 g. gave, after acid hydrolysis, 35·2% of salicylaldehyde, estimated as *p*-nitrophenylhydrazone. Theo., 33·5). It could not be distilled on account of resinification. The crude carbethoxysalicylaldehyde diphenylacetal was refluxed for 20 min. with 3*N*-NaOH, and the filtered liquid treated with a slight excess of $\mathrm{NaHCO_3}$, salicylaldehyde diphenylacetal being liberated as a thick oil, which gave a ppt. with benzidine in EtOH only slowly after the addition of AcOH.

Evidence of the Formation of an Acetal in the Reimer–Tiemann Reaction.—The following expts. were carried out on the alkaline solutions obtained by (*a*) dropping 19 c.c. of $\mathrm{CHCl_3}$ slowly into 26 g. of *p*-chlorophenol dissolved in 60 c.c. of $\mathrm{H_2O}$ containing 42 g. of KOH at 50—60°, with frequent shaking, followed by heating on the water-bath for 1 hr. and distillation of the excess of $\mathrm{CHCl_3}$, (*b*) heating a solution of *p*-chlorophenol (26 g.) and trichloroacetic acid in KOH aq. as described on p. 498. Tri-*p*-chlorophenyl orthoformate and di(chlorosalicylaldehyde) were removed by ether extraction and the alkaline solution was investigated for an acetal as follows :

(a) *Removal of free aldehyde with phenylhydrazine-*p*-sulphonic acid.* All phenolic products—chlorosalicylaldehyde, possible chlorosalicylaldehyde di-*p*-chlorophenylacetal, and unchanged chlorophenol—were liberated by the addition of a slight excess of $\mathrm{NaHCO_3}$ and extracted with $\mathrm{Et_2O}$. The evaporated extract was shaken with a solution of phenylhydrazine-*p*-sulphonic acid in $\mathrm{Na_2CO_3}$ aq. to remove free chlorosalicylaldehyde, a preliminary test with 3 g. of chlorophenol mixed with 1 g. of chlorosalicylaldehyde having proved that this could be accomplished completely in less than 1 hr. The remaining aldehyde-free oil, isolated by ether extraction, was boiled for 20 min. with 3*N*-$\mathrm{H_2SO_4}$ and then tested with *p*-nitrophenylhydrazine in AcOH. It gave 0·641 g. of chlorosalicylaldehyde-*p*-nitrophenylhydrazone (equiv. to 0·87 g. of acetal). In a second expt. the $\mathrm{NaHCO_3}$ treatment was carried out at 30—35°, and the mixture kept for $\frac{1}{2}$ hr. before ether extraction : the aldehyde-free oil then gave after hydrolysis only 0·141 g. of chlorosalicylaldehyde-*p*-nitrophenylhydrazone (0·24 g. of acetal). It was concluded that a more considerable quantity of acetal was present in the reaction product, but that it was hydrolysed to a large extent by the $\mathrm{NaHCO_3}$.

The product of the trichloroacetic acid reaction gave similarly 0·435 g. of hydrazone (equiv. to 0·59 g. of acetal).

(b) *Treatment with methylmagnesium iodide* :

$$\mathrm{HO{\cdot}C_6H_4Cl + HO{\cdot}C_6H_3Cl{\cdot}CHO + HO{\cdot}C_6H_3Cl{\cdot}CH(O{\cdot}C_6H_4Cl)_2 \xrightarrow{MeMgI} IMg{\cdot}O{\cdot}C_6H_4Cl +}$$
$$\mathrm{IMg{\cdot}O{\cdot}C_6H_3Cl{\cdot}CH(O{\cdot}MgI)Me + IMg{\cdot}O{\cdot}C_6H_3Cl{\cdot}CH(O{\cdot}C_6H_4Cl)_2 \xrightarrow{H_2SO_4} HO{\cdot}C_6H_4Cl +}$$
$$\mathrm{HO{\cdot}C_6H_3Cl{\cdot}CH(OH)Me + HO{\cdot}C_6H_3Cl{\cdot}CHO + 2HO{\cdot}C_6H_4Cl.}$$

A preliminary expt. showed that the product obtained by the action of excess of MeMgI on chlorosalicylaldehyde in ethereal solution gave no ppt. with *p*-nitrophenylhydrazine in AcOH, proving that the Grignard reagent could be used for the quantitative elimination of free aldehyde. The alkaline solution from the Reimer–Tiemann reaction was treated with a slight excess of $\mathrm{NaHCO_3}$ and extracted with $\mathrm{Et_2O}$, the extract dried with $\mathrm{Na_2SO_4}$ and run into excess of MeMgI in $\mathrm{Et_2O}$, and the product isolated by addition of $\mathrm{H_2O}$, dil. HCl, and ether extraction. The resulting oil, containing no free aldehyde, was boiled for $\frac{1}{2}$ hr. with 3*N*-$\mathrm{H_2SO_4}$ to hydrolyse acetal and then yielded 0·770 g. of chlorosalicylaldehyde-*p*-nitrophenylhydrazone (equiv. to 1·04 g. of acetal). The trichloroacetic acid process gave similarly 0·915 g. of hydrazone (1·24 g. of acetal).

(c) *Methylation with methyl sulphate* :

$$\mathrm{KO{\cdot}C_6H_4Cl + KO{\cdot}C_6H_3Cl{\cdot}CHO + KO{\cdot}C_6H_3Cl{\cdot}CH(O{\cdot}C_6H_4Cl)_2 \xrightarrow{Me_2SO_4} MeO{\cdot}C_6H_4Cl +}$$
$$\mathrm{MeO{\cdot}C_6H_3Cl{\cdot}CHO + MeO{\cdot}C_6H_3Cl{\cdot}CH(O{\cdot}C_6H_4Cl)_2 \xrightarrow{H_2SO_4} MeO{\cdot}C_6H_4Cl + MeO{\cdot}C_6H_3Cl{\cdot}CHO +}$$
$$\mathrm{2HO{\cdot}C_6H_4Cl.}$$

Methylation of salicylaldehyde in 2*N*-KOH with excess of $\mathrm{Me_2SO_4}$ at 30—40° gave a 67% yield of salicylaldehyde methyl ether, and PhOH gave a 78% yield of PhOMe. The alkaline product of the Reimer–Tiemann reaction, diluted so that the KOH was 2*N*, was similarly methylated, and the oil obtained washed with dil. NaOH aq. to remove any unchanged phenolic substances. The phenol-free oil was refluxed for $\frac{1}{2}$ hr. with 3*N*-$\mathrm{H_2SO_4}$ to hydrolyse any acetal present. Chlorophenol was isolated from the product by shaking its ethereal solution with dil. NaOH aq. and extracting the acidified alkaline solution with Et_2O. It was identified as the benzoyl derivative, m. p. 93°, and the dibromo-derivative, m. p. 90°, the latter of which was formed quantitatively and weighed. The $CHCl_3$ process gave by this method 1·527 g. of chlorodibromophenol (equiv. to 1·45 g. of acetal) and the trichloroacetic acid process 1·826 g. (1·74 g. of acetal). This seems good evidence of the formation of the acetal when it is considered that none of the methylations represented above is quantitative, and that of the acetal probably the least so.

Determination of Hydroxyl in the Resins obtained by the Trichloroacetic Acid Process.—The resins obtained from various phenols as described on p. 498 were boiled with H_2O containing a little H_2SO_4, extracted with Et_2O, dried over Na_2SO_4, recovered, and left over H_2SO_4 in a vacuum desiccator for several days. The percentage of hydroxyl in each was determined by means of Ac_2O (24 c.c.) in dry pyridine (176 c.c.). The following results were obtained:

	% OH found.				% OH found.		
Resin from	(1).	(2).	*A*.	Resin from	(1).	(2).	*A*.
Phenol	16·7	17·1	17·5	*o*-Chlorophenol	11·6	12·2	12·9
o-Cresol	14·5	14·7	15·3	*m*- ,, ...	12·6	12·0	12·9
m- ,, ...	14·6	15·4	15·3	*p*- ,, ...	12·6	12·4	12·9
p- ,, ...	14·0	14·4	15·3	Benzal chloride * ...	11·5	11·9	12·3

A = % OH in corresponding trihydroxytriphenylmethane derivative.

* This resin was obtained by refluxing 16 g. of benzal chloride, 19 g. of PhOH, and 30 g. of KOH in 200 c.c. of H_2O for 2 hr. and removing unchanged PhOH and benzal chloride by steam-distillation of the acidified mixture. % OH in dihydroxytriphenylmethane, 12·3.

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