THE REIMER–TIEMANN REACTION[1]

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CONTENTS

I. Introduction

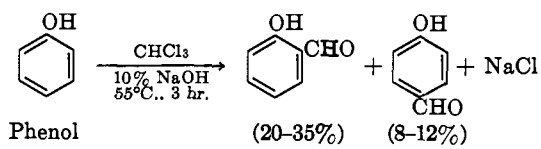
The Reimer–Tiemann reaction for the preparation of phenolic aldehydes by the action of chloroform on phenols in alkaline medium has been known and generally used for over eighty years. Substitution occurs generally ortho as well as para to the phenolic hydroxyl. The ortho:para ratio appears to depend upon the solvent (117), the substituents present (71, 72), the haloform used (5), and the nature of the cation (27, 31).

No comprehensive review of this reaction is available. Ferguson (49) devoted half a page to a brief summary of the experimental procedure; Verzele (127) expressed doubts over the then widely accepted mechanism (5) in a short review article; descriptions of some phases of the reaction have appeared in Houben-Weyl's *Methoden der organischen Chemie* (75), *Organic Syntheses* (91), and *Organic Reactions* (129).

The present review is intended to bring together the scattered literature on the Reimer–Tiemann reaction of the past eighty years. In addition to a survey of the normal reaction the review will also include a description of the two types of "abnormal" (nonaldehydic) products frequently encountered in this reaction. The literature through September 1959 has been reviewed.

A. Definition of the normal reaction

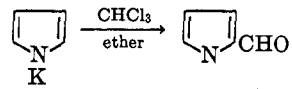
In the Reimer–Tiemann reaction a phenol is converted to an aromatic hydroxyaldehyde by warming with chloroform and aqueous alkali.



Phenol (20–35%) (8–12%)

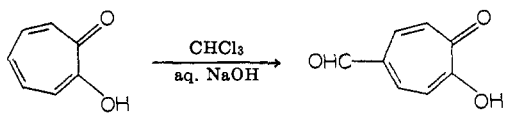
[1] *Note added in proof:* For a recent detailed investigation of the mechanism of the Reimer–Tiemann reaction, see J. Hine and J. M. van der Veen: J. Am. Chem. Soc. **81**, 6446 (1959). The conclusions reached by these investigators appear to be in agreement with the views put forth in this review.

In addition to mono- and polyhydric phenols, naphthols, and hydroxyquinolines, the introduction of an aldehyde group into pyrroles (30),



(31%)

indoles, quinoxalines, thiazoles, and tropolone (39) has also been accomplished:



Tropolone (10%)

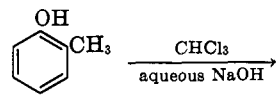
The term "normal" Reimer–Tiemann reaction, or merely Reimer–Tiemann reaction, will be reserved for that phase of the reaction in which aldehydic products are formed.

B. DEFINITION OF THE "ABNORMAL" REACTION

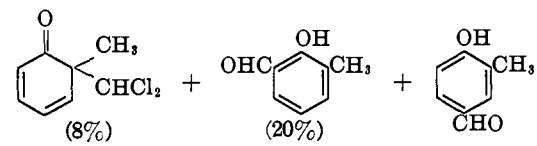
Two types of "abnormal" products may result from the reaction between phenolic compounds and chloroform in alkaline medium.

1. Cyclohexadienones

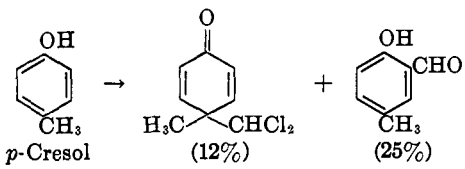
When ortho- or para-substituted phenols are subjected to the Reimer–Tiemann reaction conditions, 2,2- or 4,4-disubstituted cyclohexadienones may be obtained in addition to the normal products.



o-Cresol



(8%) (20%)

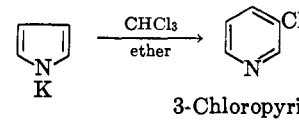


p-Cresol (12%) (25%)

Alkyl- and arylphenols, alkylnaphthols, and tetralols have been converted to cyclohexadienones.

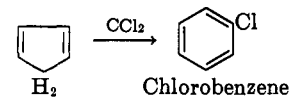
2. Ring-expansion products

A second type of "abnormal" product is frequently encountered. When Reimer–Tiemann reaction conditions are applied to a variety of five-, six-, and seven-membered ring systems, ring expansion takes place. Thus pyrrole furnishes 3-chloropyridine (19, 53, 75),



3-Chloropyridine

indoles yield chloroquinolines (47, 88, 89), and indenes furnish chloronaphthalenes and chloroazulenes (97). More recently even cyclopentadiene has been converted to chlorobenzene (29).



Chlorobenzene

C. BY-PRODUCTS

Several types of by-products may be found in the Reimer–Tiemann reaction.

1. Orthoformic esters

O-alkylation by chloroform instead of nuclear *C*-alkylation gives rise to orthoformic esters (17, 18, 46, 120, 135, 144).

$$C_6H_5OH + CHCl_3 \xrightarrow{NaOH} HC(OC_6H_5)_3$$

They are usually readily isolated in 1–3 per cent yields as neutral well-crystallized solids.

2. Hydroxy acids

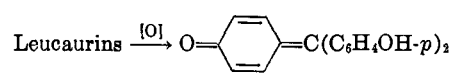
Hot alkali, especially in the presence of air, has a strong oxidizing action (85) and traces of hydroxy acids are sometimes encountered (24).

3. Triphenylmethane "resins"

Since *C*-alkylation of the phenol predominates over *O*-alkylation in the Reimer–Tiemann reaction, it is not surprising that the hydroxyaldehydes formed react further with phenol to form the well-known triphenylmethane type compounds (5).

$$HOC_6H_4CHO + 2C_6H_5OH \rightarrow HOC_6H_4CH(C_6H_4OH)_2$$

These "leucaurins," mostly of undetermined structure, were first observed as their oxidation products—the aurins—by Guareschi in 1872 (115).



4. Others

The Cannizzaro reaction of aromatic aldehydes with alkali is reported to fail with *o*- and *p*-hydroxyaldehydes (85). It appears likely that other condensations of well-established precedence (107, 136) might occur.

$$HOC_6H_4CHO \xrightarrow[OH^-]{CHCl_3} HOC_6H_4CHOHCCl_3$$

There is no report of the isolation of this type of compound or its hydrolysis product from a Reimer–Tiemann reaction.

II. Historical

In 1872 H. Schiff, in a letter to the *Berichte* from Florence, Italy, mentioned that J. Guareschi had discovered the aurin-forming color reaction when sodium phenoxides were warmed with chloroform (115). Since no experimental details were reported, it is proper that the credit for the reaction producing aldehydes is ascribed to Reimer (108, 109), who in 1876 together with Tiemann (107) was the first to isolate and identify hydroxyaldehydes as the principal reaction products of phenols and chloroform in an alkaline medium. Shortly thereafter Tiemann (120), as well as Weddige (135), isolated and identified the orthoformic esters; in 1884 von Auwers (8) isolated the chlorine-containing cyclohexadienones. The proof of structure of these latter compounds was accomplished in 1903 (14, 15, 16).

Ciamician (35) appears to have been the first to observe the ring expansion of pyrroles to chloropyridines, whose structure he established in 1882 (35). Attempts to introduce angular alkyl groups into bicyclic systems via the cyclohexadienone-producing "abnormal" reaction were initiated by Woodward in 1940 (141). Utilizing this general approach, others (44, 60, 144) remained unsuccessful in the application of this method to the synthesis of a steroid or terpene skeleton until Wenkert's (137) synthesis of a hexahydrophenanthrene possessing the A/B trans ring fusion. With the establishment of the structure of the dichloromethyl group in the cyclohexadienones (14, 15) by von Auwers, a first insight was gained into the overall mechanism of the reaction. Subsequent studies on the ortho:para ratio of aldehyde substitution as a function of alkyl- or halo-substituted phenols (71, 72) and of the metal cation employed (31) introduced views concerning chelation (31, 59, 76) into the mechanistic scheme. Armstrong and Richardson's attempts (5) to rationalize the generally low yields of the normal reaction by postulating a diarylacetal intermediate have recently been criticized (130, 131, 143). The partial identification of the occurrence of triphenylmethane "resins," which are probably mixtures of isomeric leucaurins (17, 18) and aurins, is also due to the English workers (5). The study of the rate of the alkaline hydrolysis of chloroform by Hine (67, 68, 69) set the stage for a discussion in terms of a dichlorocarbene intermediate (67, 143). Industrial application of the reaction appears to have been limited to the preparation of salicylaldehyde (75) and vanillin (128), although several German patents (58, 59) suggest that hydroxyaldehydes made via a Reimer–Tiemann reaction have been tested as dye intermediates.

III. Applications of the Reimer–Tiemann Reaction

A. The normal reaction

Direct introduction of an aldehyde group into an aromatic nucleus is limited to the Gattermann (129), Gattermann–Koch (40), Vilsmeier (51), Duff (49, 75), and Reimer–Tiemann reactions. All but the Reimer–Tiemann reaction are conducted under acidic and anhydrous conditions. Only the Gattermann and Duff reactions are applicable to phenols. Since in the Gattermann reaction the entering aldehyde group usually occupies a position para to the hydroxyl group, while the Duff reaction fails with polyhydric phenols and phenols carrying negative substituents, the Reimer–Tiemann reaction is occasionally the only method for the direct ortho formylation of phenols. Thus 2-nitrophenol (117), pyrrole, and indole, which do not furnish aldehydes in a Gattermann reaction (129), are formylated successfully under Reimer–Tiemann reaction conditions.

Using a 10:1 mole ratio of alkali to phenol to which a 2 molar excess of chloroform is added at 60–70°C. with vigorous stirring, the reaction is allowed to proceed for several hours. The sodium salt of the hydroxyaldehyde frequently separates from the concentrated solution as the reaction proceeds. Brilliant red, green, and blue colors, presumably caused by the aurins formed, are often observed. The *o*-hydroxyaldehyde is usually isolated by steam distillation of the acidified reaction mixture and separated from unchanged phenol via the bisulfite addition compound (75). In certain cases removal of the sodium salts of the phenolic aldehydes by filtration is advantageous (114, 144). Detailed instructions for the preparation of salicylaldehyde (57, 75, 133) and 2-hydroxy-1-naphthaldehyde (114) have been published.

1. Effect of solvent

Although alcohol as well as pyridine has been used as cosolvent (114, 117, 128), few generalizations appear evident. The yield of salicylaldehyde decreases (117) but that of 2-hydroxy-1-naphthaldehyde (114) increases when alcohol is used. The use of alcohol was found to have a deleterious effect in the reaction with hydroxyquinolines (27, 81) and has been claimed to suppress the formation of ortho isomers in the preparation of vanillin (128). On the other hand, pyridine is said to inhibit the formation of para isomers, to have a beneficial effect when less soluble phenols are formylated, but to cause a decrease in the yield of salicylaldehyde (114). Since pyridine, 2-methylpyridine (83), and 3-hydroxypyridine (139) react with chloroform in aqueous alkali to give ring-opening products and polymeric dyes, their use as a cosolvent must be viewed with caution.

2. *Effect of substituents*

Although it has been stated (91, 117) that phenols carrying negative groups such as nitro and carboxyl groups give lower yields than alkyl-, alkoxy-, or halophenols, data reported in support of this statement are erratic. Thus *o*-hydroxybenzoic acid furnishes 20–22 per cent of aldehydic products (5, 126), while *o*-cresol yields 10–28 per cent of hydroxyaldehydes (71, 72, 127). Since the greater reactivity of the products and their subsequent destruction through further reactions in alkaline (136, 144) as well as acid medium (71, 72) frequently obscure the yield data, competitive experiments are needed to establish relative reactivities.

The data by Hodgson (71, 72, 73, 74) and Armstrong and Richardson (5) shown in table 1 indicate the difficulties involved in discerning any pattern for substituted phenols. Internal accuracy appeared to be quite high, but the large discrepancies between the ratios indicate that reaction conditions (Hodgson used chloroform, while Armstrong and Richardson used trichloroacetic acid) materially affect the ratios. It is interesting to note further that, according to Hodgson, the reaction time had little or no effect on the ratio whereas the method of isolation did. Without more extensive data it appears unjustified to speculate on the basis for the change in the ortho:para ratio. Since no *m*-hydroxybenzaldehyde has been reported as a product from a monohydric phenol, Wheland's rule (140) stating the expected ortho:para substitution pattern for an aromatic compound containing the grouping X does not hold for *o*-halophenols.

TABLE 1

Ortho:para ratio in Reimer–Tiemann formylations of phenols using chloroform

Phenol	Aldehyde Actually Isolated Ortho:Para Ratio	Hodgson (71, 72)	Armstrong and Richardson (5)	Brady and Jakobovits (31)	
				15 *N* NaOH	2.7 *N* NaOH
Phenol	3.5	0.6	1.2	2.0	0.9
o-Cresol	2.5	0.48	0.25		
o-Chlorophenol		1.6	2.1		
m-Chlorophenol	1.0	0.84	1.3		
m-Bromophenol	1.0	0.72			
m-Iodophenol	1.0	0.78			
m-Cresol		0.85	1.1		

3. *Effect of cation*

Considerable differences in yields of *o*- and *p*-hydroxyaldehydes have been observed depending on the alkali hydroxide used. A systematic investigation is due to Brady and Jakobovits (31). These investigators determined the ortho:para ratio of products obtained from phenol in the presence of sodium, potassium, and cesium hydroxides as well as with triethylmethylammonium hydroxide. Although their reported ortho:para ratio of 2:1 with 15 *N* sodium hydroxide appears at variance with Hodgson's (71, 72) ratio of 0.6, the unmistakable trend towards increased para substitution with increasing size of the cation appears significant. The effect is attributed (31) to a decrease in the coördination of the cation with the phenoxide ion as the cation increases in size.

4. *Source of dihalocarbene*

Chloroform has generally been employed as the reagent furnishing the carbon atom for the aldehyde group. Both in homogeneous aqueous-alkaline medium (67, 69) as well as under the influence of alkali alkoxides it is clear that the reacting species appears to be dichlorocarbene (79, 118).

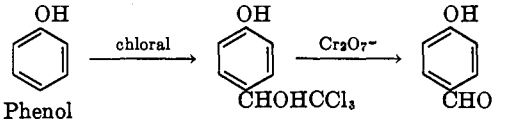
$$CHCl_3 \rightleftharpoons \bar{C}Cl_3 \rightarrow CCl_2 + Cl^-$$

The considerable differences in the yield of products (26, 27, 81, 117) with the concentration of the alkali or with the cation employed (31) may in part be due to the concentration of (solvated) dichlorocarbene available for reaction.

Trichloroacetic acid, which has also been employed as a source of dichlorocarbene in aqueous-alkaline medium (3, 5), has recently been found to furnish the dihalocarbene in organic solvents under essentially neutral conditions (134).

$$CCl_3COONa \xrightarrow{\text{1,2-dimethoxyethane}} CCl_2$$

Chloral, quoted (91) as having been used in a Reimer–Tiemann synthesis, converts the phenol to the corresponding trichlorocarbinol. Subsequent oxidation by chromate is needed to prepare the aldehyde. Both



hydroxy aldehydes as well as hydroxy acids have been isolated from the reaction of trichloronitromethane with phenol (24).

Bromoform, which has been used instead of chloroform both in the normal reaction (71, 72) and in the formation of cyclohexadienones (9) and ring-expansion products (98), appears to offer no particular advantages.

5. *Alkylphenols (table 2)*

There appears to be no limitation to the formylation of alkylphenols via the Reimer–Tiemann reaction. All of the cresols (3, 33, 71, 72, 127, 186) and four of the six isomeric xylenols (4, 11, 12, 16, 75), as well as 2,4,5-trimethylphenol (8), furnish normal products in yields ranging from 5 to 35 per cent. Although 4-isobutylphenol (42) and 4-*tert*-butylphenol (75) have also

TABLE 2

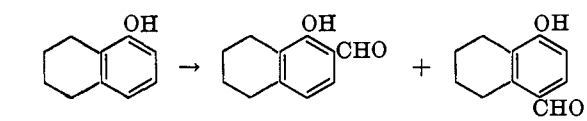
Hydroxyaldehydes obtained from phenols and alkylphenols

Phenol	Product	Yield	References
		per cent	
Phenol	Salicylaldehyde	37. 25	(3. 5. 24. 49. 57. 71. 72.
	p-Hydroxybenzaldehyde	8	75. 117. 131. 133)
o-Cresol	2-Hydroxy-3-methylbenzaldehyde	20	(71. 72. 127)
	4-Hydroxy-3-methylbenzaldehyde	8	
m-Cresol	2-Hydroxy-6-methylbenzaldehyde	—	(33. 71. 72. 86. 127)
	2-Hydroxy-4-methylbenzaldehyde	9	
	4-Hydroxy-2-methylbenzaldehyde	—	
p-Cresol	2-Hydroxy-5-methylbenzaldehyde	25	(3. 127)
3,5-Dimethylphenol	4,6-Dimethyl-2-hydroxybenzaldehyde	Low	(11)
	2,6-Dimethyl-4-hydroxybenzaldehyde	Low	
3,4-Dimethylphenol	4,5-Dimethyl-2-hydroxybenzaldehyde*	—	(12)
2,5-Dimethylphenol	3,6-Dimethyl-2-hydroxybenzaldehyde		(4. 16)
	2,5-Dimethyl-4-hydroxybenzaldehyde		
	2,5-Dimethyl-3-formyl-4-hydroxybenzaldehyde*		
2,4-Dimethylphenol	3,5-Dimethyl-2-hydroxybenzaldehyde	Low	(4. 16. 75)
2,4,5-Trimethylphenol	2-Hydroxy-3,5,6-trimethylphenol	5	(8)
2-Isopropyl-5-methylphenol (thymol)	4-Hydroxy-5-isopropyl-2-methylbenzaldehyde	11	(21. 80)
	2-Hydroxy-3-isopropyl-6-methylbenzaldehyde	17	
	3-Formyl-4-hydroxy-5-isopropyl-2-methylbenzaldehyde*	—	
5-Isopropyl-2-methylbenzaldehyde (carvacrol)	2-Hydroxy-6-isopropyl-3-methylbenzaldehyde	—	(21. 86. 93)
	4-Hydroxy-6-isopropyl-3-methylbenzaldehyde	Trace	
4-Isobutylphenol	2-Hydroxy-5-isobutylbenzaldehyde		(42)
4-*t*-Butylphenol	5-*t*-Butyl-2-hydroxybenzaldehyde		(75)
5,6,7,8-Tetrahydro-1-naphthol	5,6,7,8-Tetrahydro-1-hydroxy-2-naphthaldehyde	9	
	5,6,7,8-Tetrahydro-1-hydroxy-4-naphthaldehyde	2	(144)
5,6,7,8-Tetrahydro-2-naphthol	5,6,7,8-Tetrahydro-3-hydroxy-2-naphthaldehyde	Trace	(6. 141)
	5,6,7,8-Tetrahydro-1-hydroxy-2-naphthaldehyde	20. 50	
5,6,7,8-Tetrahydro-1-methyl-2-naphthol	5,6,7,8-Tetrahydro-2-hydroxy-1-methyl-3-naphthaldehyde	20	(64)
2-Naphthol	2-Hydroxy-1-naphthaldehyde	40–72	(78. 82. 113. 114)
4-Hydroxybiphenyl	3-Formyl-4-hydroxybiphenyl	—	(64)
4-Hydroxybiphenylmethane	3-Formyl-4-hydroxybiphenylmethane	11	(64)

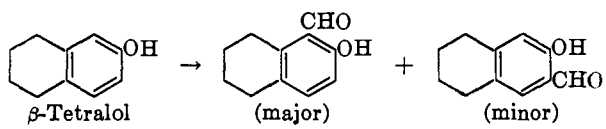
* The structure of this compound has not been rigidly proven.

been formylated successfully, no systematic study has been made of the reaction with alkylphenols from the point of view of steric hindrance or the ortho:para ratio.

Both *ar*-α-tetralol and *ar*-β-tetralol furnish the two isomers (6, 141, 144) in addition to the desired "abnormal" products,



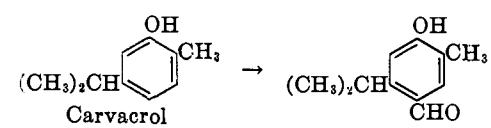
α-Tetralol (major) (minor)



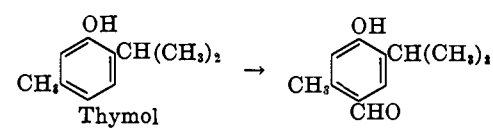
β-Tetralol (major) (minor)

in expected contrast to α- and β-naphthol. Whereas α-naphthol has not yet been successfully formylated (77), β-naphthol (78, 82, 113, 114) furnishes the 1-aldehydo isomer in high yield.

Since no accurate yield nor data on isomer ratio are available for the open-chain analogs of α- and β-tetralol, no comparison can be made about the effect of this fused-ring system on the isomer ratio. Carvacrol (21, 86, 93) and thymol (21, 80) are said to give a preponderance of the para isomer, although complete characterization of all of the products is lacking.

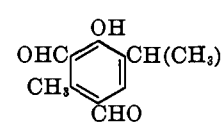


Carvacrol



Thymol

A dialdehyde, presumably having the following structure



has been described by Kobek (78, 80).

6. *Halophenols (table 3)*

All four types of halophenols have been formylated successfully (50, 71, 72, 73, 74). The *o*-fluoro- (50) and *o*-bromophenols give considerably better yields than their para isomers. The ortho:para ratio of a series of ortho- and meta-substituted chloro-, bromo-, and iodophenols has been determined (71, 72), but complete characterization and proof of structure of all of the isomers have not yet been recorded.

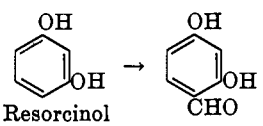
TABLE 3

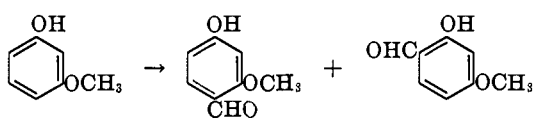
Hydroxyaldehydes obtained from halophenols using chloroform

Phenol	Product	Yield	References
		per cent	
o-Fluorophenol	3-Fluoro-2-hydroxybenzaldehyde	13	(50)
	3-Fluoro-4-hydroxybenzaldehyde	15	
p-Fluorophenol	5-Fluoro-2-hydroxybenzaldehyde	8	(50)
o-Chlorophenol	3-Chloro-2-hydroxybenzaldehyde	—	(71, 72)
	3-Chloro-4-hydroxybenzaldehyde (*o*:*p* = 1.6)	—	
m-Chlorophenol	4-Chloro-2-hydroxybenzaldehyde	19	(73)
	2-Chloro-4-hydroxybenzaldehyde	19	
p-Chlorophenol	5-Chloro-2-hydroxybenzaldehyde	53	(131)
o-Bromophenol	3-Bromo-2-hydroxybenzaldehyde	13–17	(71, 72, 117)
	3-Bromo-4-hydroxybenzaldehyde	4–5	
m-Bromophenol	4-Bromo-2-hydroxybenzaldehyde	19	(74)
	2-Bromo-4-hydroxybenzaldehyde	18	
p-Bromophenol	5-Bromo-2-hydroxybenzaldehyde	—	(75)
o-Iodophenol	2-Hydroxy-3-iodobenzaldehyde	—	
	4-Hydroxy-3-iodobenzaldehyde (*o*:*p* = 1.07)	—	(72)
m-Iodophenol	2-Hydroxy-4-iodobenzaldehyde	15	(71, 72)
	4-Hydroxy-2-iodobenzaldehyde	15	
4-Chloro-2-naphthol	4-Chloro-2-hydroxy-1-naphthaldehyde	22	(32)
5,6,7,8-Tetrahydro-1-bromo-2-naphthol	5,6,7,8-Tetrahydro-4-bromo-3-hydroxy-2-naphthaldehyde	12	(64)
4′-Chloro-4-hydroxybiphenylmethane	4′-Chloro-3-formyl-4-hydroxybiphenylmethane	10	(94)

7. *Hydroxy- and alkoxyphenols (table 4)*

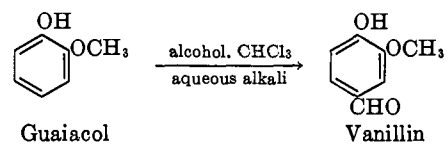
Hydroquinone (124) and resorcinol (122, 123), as well as their monomethyl ethers (125) and guaiacol (122), have been formylated successfully.





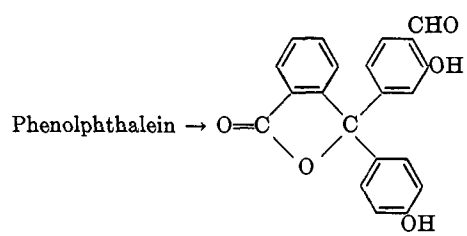
In addition to one monoaldehyde (122, 123, 125) and two isomeric monoaldehydes, reported to be formed from resorcinol and resorcinol methyl ether, respectively, both compounds are said to furnish traces of dialdehydes.

The yield of vanillin from guaiacol is said to be affected favorably by the addition of alcohol (128).



Guaiacol — Vanillin

The highest yield of normal product (75 per cent) is recorded for the Reimer–Tiemann reaction with phenolphthalein (75, 77).



It is perhaps significant that a combination of (*1*) high molecular weight, (*2*) structure, and (*3*) solubility inhibits side-reactions (formation of leucaurins, cyclohexadienones, and orthoformic esters).

TABLE 4

Hydroxyaldehydes obtained from hydroxy- and alkoxyphenols

Phenol	Product	Yield	References
		per cent	
3-Hydroxyphenol	2,4-Dihydroxybenzaldehyde	23	(122, 123)
4-Hydroxyphenol	2,5-Dihydroxybenzaldehyde	—	(124)
2-Methoxyphenol (guaiacol)	4-Hydroxy-3-methoxybenzaldehyde (vanillin)	—	(122, 128)
	2-Hydroxy-3-methoxybenzaldehyde	—	
3-Methoxyphenol	4-Hydroxy-2-methoxybenzaldehyde	25	(125)
	2-Hydroxy-4-methoxybenzaldehyde	—	
	α-Dialdehyde	—	
	β-Dialdehyde	—	
4-Methoxyphenol	2-Hydroxy-5-methoxybenzaldehyde	50–65	(60a, 124)
4-Methoxy-2-methylphenol	2-Hydroxy-5-methoxy-3-methylbenzaldehyde	13	(142)
3,5-Dimethoxyphenol	2,6-Dimethoxy-4-hydroxybenzaldehyde	—	(63)

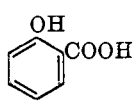
TABLE 5

Hydroxyaldehydes obtained from phenols substituted with carboxy and sulfonic acid groups

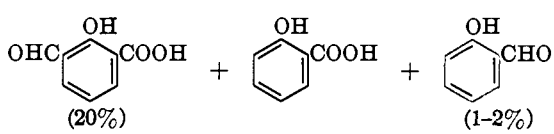
Phenol	Product	Yield	References
		per cent	
Salicylic acid	5-Formyl-2-hydroxybenzoic acid	17	(5,72,111)
	3-Formyl-2-hydroxybenzoic acid	—	(126)
p-Hydroxybenzoic acid	3-Formyl-4-hydroxybenzoic acid	15,20	(5,111,126)
m-Hydroxybenzoic acid	*x*-Formyl-3-hydroxybenzoic acid	7	(5)
4-Hydroxy-1,3-benzenedicarboxylic acid	5-Formyl-4-hydroxy-1,3-benzenedicarboxylic acid	—	(109)
5-Hydroxy-1,3-benzenedicarboxylic acid	2-Formyl-5-hydroxy-1,3-benzenedicarboxylic acid	—	(109)
1-Naphthol-4-sulfonic acid	2-Formyl-1-naphthol-4-sulfonic acid	—	(58,59)
2-Naphthol-6-sulfonic acid	1-Formyl-2-naphthol-6-sulfonic acid	—	(58,59)
2-Naphthol-7-sulfonic acid	1-Formyl-2-naphthol-7-sulfonic acid	—	(58,59)
2-Naphthol-3,6-disulfonic acid	1-Formyl-2-naphthol-3,6-disulfonic acid	—	(58,59)
2-Naphthol-6,8-disulfonic acid	1-Formyl-2-naphthol-6,8-disulfonic acid	—	(58,59)
2-Hydroxy-3-naphthoic acid	3-Carboxy-2-hydroxy-1-naphthaldehyde	—	(58,59)
3-Carboxy-2-naphthol-6-sulfonic acid	3-Carboxy-1-formyl-2-naphthol-6-sulfonic acid	—	(58,59)
1-Naphthol-2-sulfonic acid	4-Formyl-1-naphthol-2-sulfonic acid	—	(58,59)
1-Naphthol-4,8-disulfonic acid (as the 1,8-sulfone)	2-Formyl-1-naphthol-4,8-disulfonic acid	—	(58,59)
1-Naphthol-4,7-disulfonic acid	2-Formyl-1-naphthol-4,7-disulfonic acid	—	(58,59)
2-Naphthol-3,7-disulfonic acid	1-Formyl-2-naphthol-3,7-disulfonic acid	—	(58,59)
o-Hydroxybenzenesulfonic acid	5-Formyl-2-hydroxybenzenesulfonic acid	—	(58,59)

8. Phenols carrying carboxyl and sulfonic acid groups (table 5)

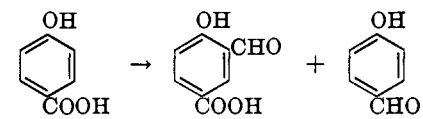
All of the three isomeric hydroxybenzoic acids furnish aldehydes in yields ranging from 7 to 20 per cent (5, 55, 72, 75, 109, 111, 126). The low yields are apparently due in part (144) to the competition between the (slower) nuclear substitution reaction and the further reactions of the products in the presence of alkali and chloroform. When salicylic acid is formylated (126), small amounts (1–2 per cent) of salicylaldehyde are formed.



Salicylic acid



p-Hydroxybenzoic acid likewise furnishes traces of *p*-hydroxybenzaldehyde (but no salicylaldehyde).



These results strongly suggest (126) direct replacement of carboxyl by the carbon atom of the chloroform moiety rather than (*a*) prior decarboxylation or (*b*) subsequent decarboxylation. Even two carboxyl groups do not prevent nuclear formylation, both 4- and 5-hydroxyisophthalic acid yielding the corresponding aldehydo compounds (109).

In a series of patents (58, 59) the successful formylation of naphtholmonosulfonic acid and naphtholdisulfonic acid was reported. No analytical data, yields, or structure proofs are available.

9. Heterocyclic phenols (table 6)

Several hydroxyquinolines and one hydroxythiazole have been formylated successfully. Thus, 2-hydroxy-4-methylthiazole furnishes the corresponding aldehyde in low yield (94).

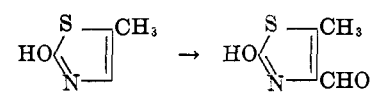


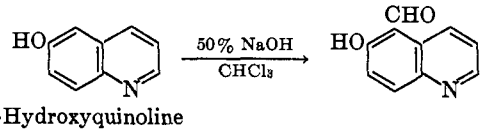
TABLE 6

Hydroxyaldehydes obtained from heterocyclic phenols

Compound	Product	Yield	References
		per cent	
4-Hydroxyquinoline	4-Hydroxyquinoline-3-aldehyde	—	(27)
6-Hydroxyquinoline	6-Hydroxyquinoline-5-aldehyde	—	(26)
7-Hydroxyquinoline	7-Hydroxyquinoline-8-aldehyde	38	(81)
8-Hydroxyquinoline	8-Hydroxyquinoline-5-aldehyde	30	
	8-Hydroxyquinoline-7-aldehyde	10	(84,117)
2,4-Dihydroxyquinoline	2,4-Dihydroxyquinoline-3-aldehyde	—	(7)
2-Methyl-4-hydroxyquinoline	2-Methyl-4-hydroxyquinoline-3-aldehyde	50	(38)
2-Hydroxy-4-methylthiazole	2-Hydroxy-4-methylthiazole-3-aldehyde	Trace	(94)
2-Hydroxy-3-carboxycarbazole	2-Hydroxy-3-carboxycarbazole-1-aldehyde	—	(75)

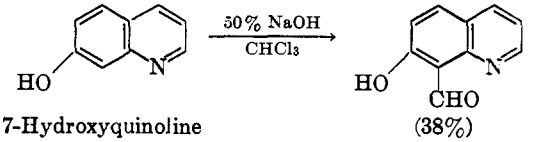
Well-characterized are the hydroxyquinolines of Bobranski (26, 27, 81), who found that sodium hydroxide but not potassium hydroxide gave the best results in very concentrated *aqueous* solutions.

In agreement with the results with β-naphthol (113, 114), 6-hydroxyquinoline furnished 5-formyl-6-hydroxy-



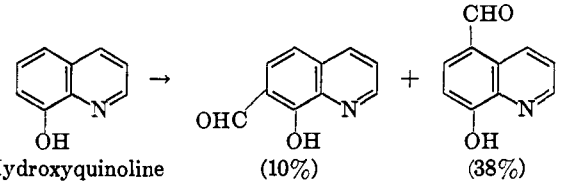
6-Hydroxyquinoline

quinoline (26), while 7-hydroxyquinoline gave the corresponding aldehyde in 38 per cent yield (81).



7-Hydroxyquinoline (38%)

Of considerable interest is the fact that 8-hydroxyquinoline is reported (117) to give the two normal products in fair yields in sharp contrast to the behavior of α-naphthol, from which no aldehydic products have



8-Hydroxyquinoline (10%) (38%)

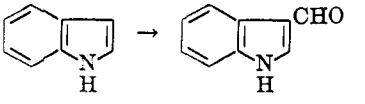
been isolated to date (78). Another interesting report concerns the successful formylation of 4-hydroxyquinoline (27) and 4-hydroxy-3-methylquinoline (81) to give the *o*-hydroxyaldehydes. Rigid structure proof

has not yet been furnished and is essential, since none of the three isomeric hydroxypyridines have been formylated successfully. For instance, 2-formyl-3-hydroxypyridine, a known (62) substance, could not be isolated from a Reimer–Tiemann reaction involving 3-hydroxypyridine. Instead, an apparently polymeric-amphoteric substance of unknown constitution (139) was formed. This is in accord with the findings of König (83), who observed and studied the ring opening of pyridines in alkaline medium. It appears that the additional stabilization by the second aromatic ring (in the quinolines) is needed for successful formylation.

10. Nonphenolic heterocyclic compounds (table 7)

Pyrroles (14, 53, 73, 75, 106), indoles (25, 30, 47, 48, 89), and a glyoxaline (66) are representatives of heterocyclic compounds reacting successfully under Reimer–Tiemann reaction conditions.

Pyrrole furnishes pyrrole-2-aldehyde (75), while indole gives the expected indole-3-aldehyde (30).



Indole Indole-3-aldehyde

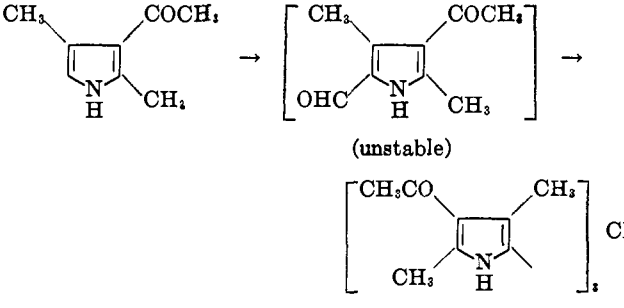
TABLE 7

Heterocyclic aldehydes prepared via the Reimer–Tiemann reaction

Starting Compound	Product	Yield	References
		per cent	
Pyrrole	Pyrrole-2-aldehyde	31	(19,53,53a,75)
2,5-Dimethylpyrrole	2,5-Dimethylpyrrole-3-aldehyde	13	(106)
Indole	Indole-3-aldehyde	31	(30,47)
2-Methylindole	2-Methylindole-3-aldehyde	47	(30,48)
5-Methylindole	5-Methylindole-3-aldehyde	27	(30)
7-Methylindole	7-Methylindole-3-aldehyde	31	(30)
5-Methoxyindole	5-Methoxyindole-3-aldehyde	30	(89)
7-Methoxyindole	7-Methoxyindole-3-aldehyde	20	(89)
2-Phenylindole	2-Phenylindole-3-aldehyde	52	(25)
2-Mercapto-4-methylglyoxaline	5-Formyl-2-mercapto-4-methylglyoxaline	—	(60)

The yield data are again obscure, since competing reactions—i.e., ring expansion—take place.

3-Acetyl-2,4-dimethylpyrrole when subjected to Reimer–Tiemann reaction conditions (103) furnishes a tripyrryl derivative (52), undoubtedly the result of condensation of the aldehyde:



The lack of further condensation could well explain the 52 per cent yield observed when 2-phenylindole is converted to 2-phenylindole-3-aldehyde (25).

No study has been made of the relative ratio of nor-

TABLE 8

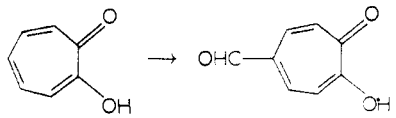
Reimer–Tiemann reaction with miscellaneous phenols

Phenol	Product	Yield	References
		per cent	
o-Nitrophenol	2-Hydroxy-3-nitrobenzaldehyde	11	(117)
m-Nitrophenol	2-Hydroxy-4-nitrobenzaldehyde	3	(5)
p-Nitrophenol	2-Hydroxy-5-nitrobenzaldehyde	—	(117)
2-Hydroxycinnamic acid	3-Formyl-2-hydroxycinnamic acid	10	(117)
β-(*p*-Hydroxyphenyl)propionic acid	β-(3-Formyl-4-hydroxyphenyl)propionic acid	13	(144)
2-Hydroxyanthraquinone	2-Hydroxyanthraquinone-1-aldehyde	25	(117)

mal products to ring-expansion products as a function of substitution (either from the electronic or from the steric point of view).

11. Miscellaneous compounds (table 8)

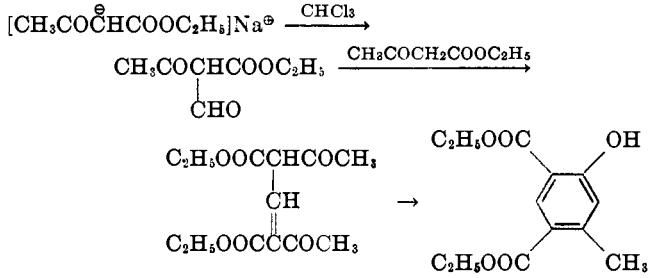
The recent report (39) that tropolone furnished tropolone-4-aldehyde in 10 per cent yield when treated with chloroform in dilute aqueous alkali is of considerable interest. The failure to achieve nuclear alkylation via the Gattermann, Kolbe–Schmidt, or chloro-



Tropolone

methylation reaction shows the occasional value of this (Reimer–Tiemann) substitution reaction conducted under mild alkaline conditions. Addition of dichlorocarbene, followed by ring expansion (29, 98) which might have been expected, can apparently be suppressed by working in dilute aqueous solutions.

When acetoacetic ester is treated with chloroform or trichloroacetic acid an aromatic substance is isolated to which the structure diethyl 4-hydroxy-6-methylisophthalate has been assigned (95). Formylation of the carbanion of acetoacetic ester, followed by inter- and intramolecular aldol condensations, provides a possible explanation of the formation of this reaction product.



B. THE ABNORMAL REACTION

1. Cyclohexadienones, pyrrolenines, and indolenines (table 9)

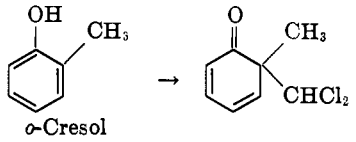
When *o*- and *p*-alkyl- or *o*- and *p*-arylphenols, 2,5-dialkylpyrroles, and 2,3-dialkylindoles are treated

TABLE 9

Cyclohexadienones obtained via a Reimer–Tiemann reaction

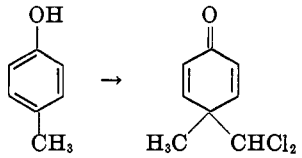
Phenol	Product	Yield	References
		per cent	
o-Cresol	2-Dichloromethyl-2-methyl-3,5-cyclohexadienone	8	(14)
p-Cresol	4-Dichloromethyl-4-methyl-2,5-cyclohexadienone	12	(13,14)
2,4-Dimethylphenol	4-Dichloromethyl-2,4-dimethyl-2,5-cyclohexadienone	30	(13)
3,4-Dimethylphenol	4-Dichloromethyl-3,4-dimethyl-2,5-cyclohexadienone	28	(13)
2,5-Dimethylphenol	2-Dichloromethyl-3,5-dimethyl-3,5-cyclohexadienone	1.5	(13,142)
2,6-Dimethylphenol	2-Dichloromethyl-2,6-dimethyl-3,5-cyclohexadienone	19	(142)
2,4,5-Trimethylphenol	4-Dichloromethyl-2,4,5-trimethyl-2,5-cyclohexadienone	42	(8,9,13)
2,4,6-Trimethylphenol	2-Dichloromethyl-2,4,6-trimethyl-3,5-cyclohexadienone	46	
	4-Dichloromethyl-2,4,6-trimethyl-3,5-cyclohexadienone	21	(20,144)
4-Methoxy-2-methylphenol	2-Dichloromethyl-2-methyl-4-methoxy-3,5-cyclohexadienone	8	(142)
4-Hydroxybiphenyl	4-Dichloromethyl-4-phenyl-2,5-cyclohexadienone	6	(62)
1-Methyl-2-naphthol	1-Dichloromethyl-1-methyl-2-keto-1,2-dihydronaphthalene	80	(22,44)
1-Allyl-2-naphthol	1-Allyl-1-dichloromethyl-2-keto-1,2-dihydronaphthalene	47	(44)
1-(3-Chlorobutenyl)-2-naphthol	1-Dichloromethyl-1-(3-chloro-2-butenyl)-2-keto-1,2-dihydronaphthalene	35	(44)
5,6,7,8-Tetrahydro-1-naphthol	9-Dichloromethyl-1-keto-$\Delta^{2,4}$-hexahydronaphthalene	3	(144)
5,6,7,8-Tetrahydro-2-naphthol	10-Dichloromethyl-2-keto-$\Delta^{1,9,3,4}$-hexahydronaphthalene	12	(141)
5,6,7,8-Tetrahydro-2-methoxy-1-naphthol	9-Dichloromethyl-1-keto-2-methoxy-$\Delta^{2,4}$-hexahydronaphthalene	1	(142)
5,6,7,8-Tetrahydro-1-methyl-2-naphthol	10-Dichloromethyl-2-keto-1-methyl-$\Delta^{1,9,3,4}$-hexahydronaphthalene	13	(64)
5,6,7,8-Tetrahydro-1-bromo-2-naphthol	10-Dichloromethyl-1-bromo-2-keto-$\Delta^{1,9,3,4}$-hexahydronaphthalene	4.5	(64)
β-(*p*-Hydroxyphenyl)propionic acid	Ethyl β-(1-dichloromethyl-2,5-cyclohexadien-4-one) propionate	17	(142)
2,5-Dimethylpyrrole	2-Dichloromethyl-2,5-dimethylpyrrolenine	—	(106)
2,3-Dimethylindole	3-Dichloromethyl-2,3-dimethylindolenine	—	(104)
Tetrahydrocarbazole	11-Dichloromethyltetrahydrocarbazolenine	—	(104)
4-Methyl-1-naphthol	4-Dichloromethyl-5-keto-2*a*,5-dihydroacenaphthene	14	(56,137)
5-Acenaphthol	2*a*-Dichloromethyl-5-keto-2*a*,5-dihydroacenaphthene	6	(56)

with alkali and chloroform, nuclear substitution at the carbon atom carrying the substituent may take place. An aromatic system is transformed into a nonaromatic system under dilute alkaline conditions. Thus *o*-cresol furnishes 2-dichloromethyl-2-methyl-3,5-cyclohexadienone in 8 per cent yield (13),



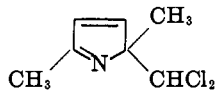
o-Cresol

while *p*-cresol gives 4-dichloromethyl-4-methyl-2,5-cyclohexadienone in slightly better yield (14).

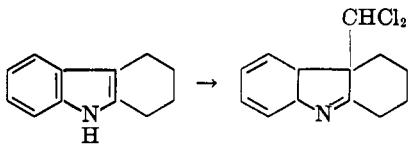


p-Cresol

Likewise 2,5-dimethylpyrrole (106) furnishes a chlorine-containing base possibly possessing a pyrrolenine structure,



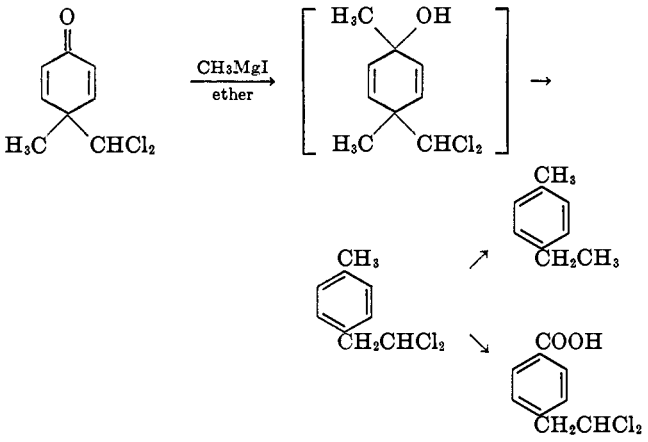
while tetrahydrocarbazole appears to yield an indolenine (105).



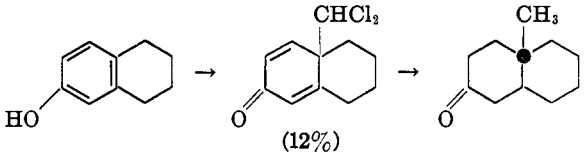
Tetrahydrocarbazole

Although structure proof of the pyrrolenines and indolenines is lacking, the structure of the cyclohexadienones rests on a sound basis.

Von Auwers, who was the first to isolate these chloroketones among the normal products of Reimer–Tiemann reactions (8, 9, 10, 11, 12, 13, 16), assigned a structure to the product from *p*-cresol on the basis of the following reactions (14, 15):

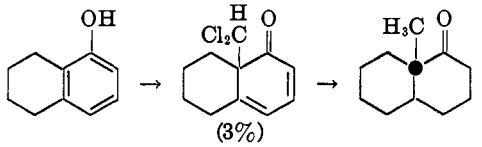


Transformations of the cyclohexadienones to compounds whose structures are known by independent syntheses have further strengthened the structural assignment. Thus Woodward (141) was able to transform a tetralol into *trans*-10-methyldecalone-2,



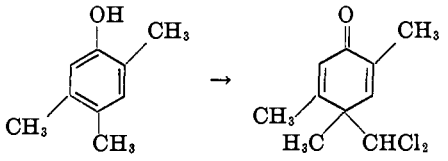
(12%)

while more recently its isomer was similarly transformed into *trans*-9-methyldecalone-1 (144).



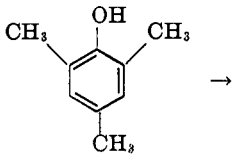
(3%)

The generality of this reaction with alkylphenols appears to be well established. In addition to *o*- and *p*-cresol (13, 14), four of the six isomeric xylenols (13, 142) and two of the six trimethylphenols (13, 20, 142) have been converted to cyclohexadienones. Although only the para isomer has been isolated from 2,4-dimethylphenol and 2,4,5-trimethylphenol, it has

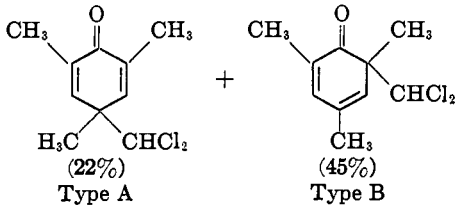


2,4,5-Trimethylphenol

recently been possible (20, 144) to prove the presence of both 2,2- and 4,4-disubstituted cyclohexadienones in the neutral product resulting from the reaction of mesitol with chloroform and alkali.



Mesitol

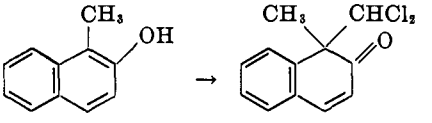


(22%) Type A (45%) Type B

Ultraviolet absorption spectroscopy has proved to be a valuable aid in the rapid identification of the two isomeric structures. Thus structures of type A (cross-conjugated) show maximum absorption at 232–242 mμ with only 2–3 mμ bathochromic shifts due to the presence of an additional alkyl group. The linearly

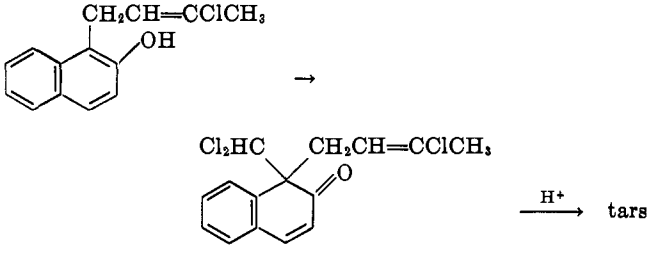
conjugated system of type B, on the other hand, shows maximum absorption at 299–348 mμ (41, 144), the considerable spread being due to the expected 10–12 mμ bathochromic shifts caused by alkyl substituents.

Several different types of alkyl- and halotetralols (64), alkylnaphthols (22, 44, 56, 137), acenaphthol (44), and phenanthrols (60) have been converted successfully into dichloroketones. In some cases the yields have exceeded those observed in the formation of the normal products. Thus 1-methyl-2-naphthol (22, 44) furnishes the naphthenolone in 80 per cent yield.

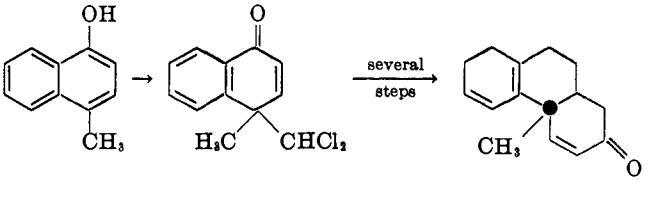


Attempts to utilize the reaction for the synthesis of steroid or terpenoid substances have only recently met with success. Neither Woodward's original scheme of introducing an angular methyl group into a tetralol (141) nor Wynberg and Johnson's (144) alternate approach was successful when applied to polycyclic nuclei.

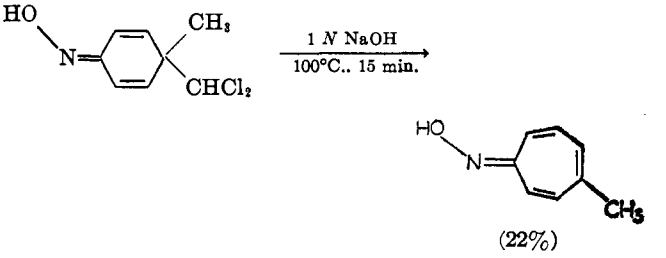
Dodson and Webb (44) failed to effect cyclization of the abnormal product from 1-(3-chlorobutenyl)-2-naphthol,



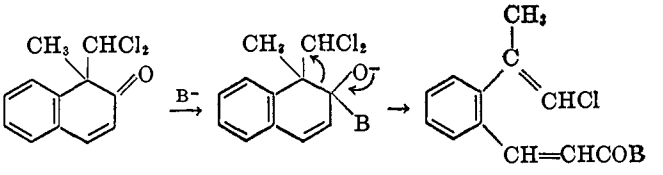
while the hexahydrophenanthrene prepared by Gibson (60) has apparently failed to furnish the desired tricyclic skeleton. Starting with 4-methyl-1-naphthol, however, Wenkert and Stevens (137) have recently prepared a hexahydrophenanthrene possessing the natural trans A/B ring fusion of aromatic tricyclic diterpenes.



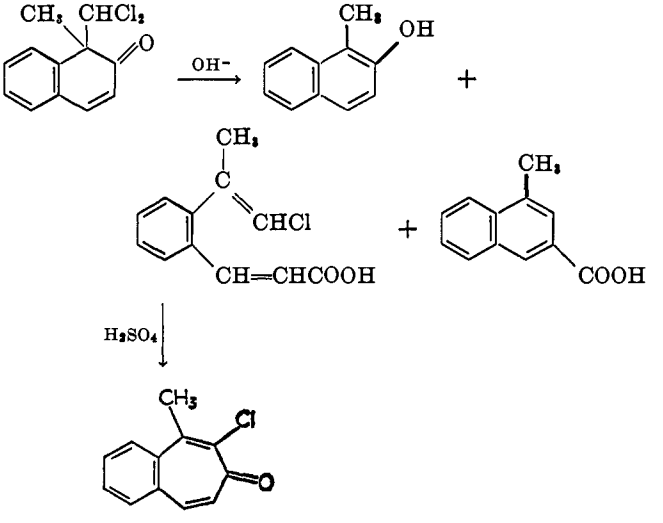
Although these compounds are surprisingly stable under many different conditions (13), interesting rearrangements have been observed. Thus the oxime of 4-dichloromethyl-4-methyl-2,5-cyclohexadienone has been transformed into 4-methyltropone oxime (116).



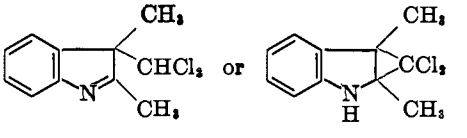
The qualitative difference in ease of decomposition between 2,2- and 4,4-disubstituted cyclohexadienones observed by von Auwers (13) has found expression recently by Wenkert and Stevens (137), who postulated a sequence terminating in the ring opening of the cyclic ketone:



Confirmation of these ideas has been obtained by Wenkert (136a), who has isolated the following products when the naphthenolone was treated with base:



The importance of the base-catalyzed reversal and acid-catalyzed ring expansion for the determination of the reaction conditions and isolation of the cyclohexadienones is immediately apparent. The dichloromethylpyrrolenines and indolenines of Plancher (104, 105, 106) deserve careful study, since the isomeric true dichlorocarbene-adduct structure, recently made more plausible by the work of Parham (98), cannot be ruled out.



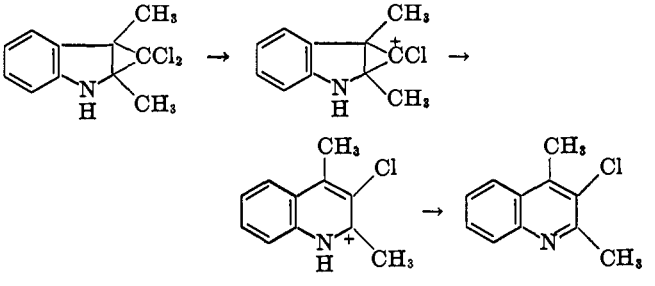
The cyclopropane structure could give rise to the chloroquinolines under basic conditions in the same

TABLE 10

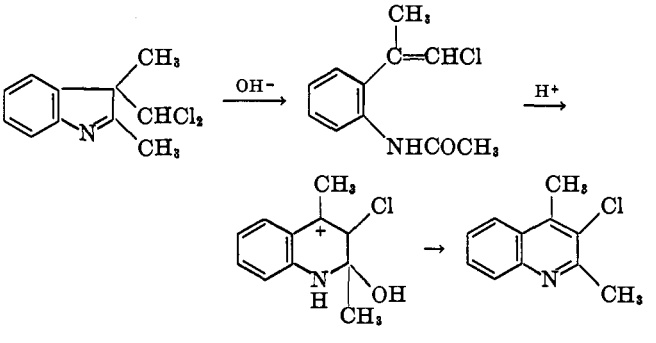
Ring-expansion products of the Reimer–Tiemann reaction

Starting Material	Reagent	Product	Yield	References
			per cent	
Pyrrole	Chloroform	3-Chloropyridine	13	(2,34,35)
	Bromoform	3-Bromopyridine	4	(2,34,35)
	Benzal chloride	3-Phenylpyridine	1	(2,34,36)
	Methylene iodide	Pyridine	2.5	(2,34,43)
2,5-Dimethylpyrrole	Chloroform	3-Chloro-2,6-dimethylpyridine		(28)
	Bromoform	3-Bromo-2,6-dimethylpyridine	15	(28)
2,3-Dimethylpyrrole	Bromoform	Dialkylbromopyridine	10	(28)
Indole	Chloroform	3-Chloroquinoline	9	(30,47,104)
	Bromoform	3-Bromoquinoline	10	(47)
2-Methylindole	Chloroform	3-Chloro-2-methylquinoline	—	(30)
3-Methylindole	Chloroform	3-Chloro-4-methylquinoline	—	(88)
5-Methylindole	Chloroform	3-Chloro-6-methylquinoline	—	(30)
7-Methylindole	Chloroform	3-Chloro-8-methylquinoline	18	(30)
5-Methoxyindole	Chloroform	3-Chloro-6-methoxyquinoline	—	(89)
1-Methoxyindole	Chloroform	3-Chloro-8-methoxyquinoline	—	(89)
2-Phenylindole	Chloroform	3-Chloro-2-phenylquinoline	—	(25)
Indene	Chloroform	2-Chloronaphthalene	65	(97,98)
	Bromoform	2-Bromonaphthalene	51	(98)
1-Methylindene	Chloroform	2-Chloro-1-methylnaphthalene	—	(98)
2-Methylindene	Chloroform	2-Chloro-3-methylnaphthalene	37	(100)
Ethoxyindene	Bromoform	2-Bromo-3-ethoxynaphthalene	34	(100)
Isopropylindene	Chloroform	2-Chloro-4-isopropylnaphthalene	38	(100)
2(3)-Chloroindene	Chloroform	1,2-Dichloronaphthalene	5	(100)
3-Phenylindene	Bromoform	2-Bromo-1-phenylnaphthalene	5	(100)
Cyclopentadiene	Chloroform	Chlorobenzene	—	(29)
Cycloheptatriene	Chloroform	1-Chlorobenzocyclobutene	10	(29)

fashion that chloronaphthalenes are formed from the indene adducts (98).

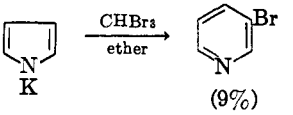


The transformation of the dichloromethylindolenine to a quinoline might conceivably proceed via the base-catalyzed ring opening followed by the acid-catalyzed ring closure according to Wenkert (137).

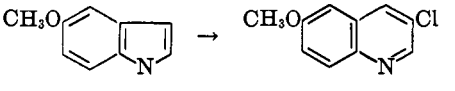


2. Ring-expansion products (table 10)

In 1881 Ciamician (35) observed and subsequently proved that the potassium salt of pyrrole, when heated with chloroform or bromoform in ether, furnished a β-halopyridine.



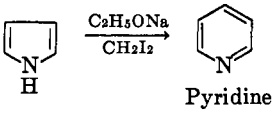
Subsequent investigators (2, 34, 35, 36, 89, 104) found that even under normal (aqueous) Reimer–Tiemann reaction conditions, ring-expansion products could be isolated in addition to normal products. In 1950 Alexander (2), investigating the reaction in some detail, confirmed the findings of earlier workers but was unable to improve the low (1–25 per cent) yields of this conversion. Pyrroles, alkylpyrroles, and alkyl- and alkoxyindoles were found to furnish ring-expansion products. Thus 5-methoxyindole gives 3-chloro-6-methoxyquinoline in 25 per cent yield (89).



5-Methoxyindole

The normal product, 5-methoxyindole-3-aldehyde, is formed in 30 per cent yield.

If methylene iodide is used instead of a haloform, traces of pyridine can be isolated (2, 34, 43).

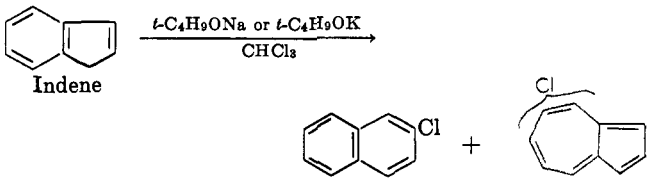


Pyridine

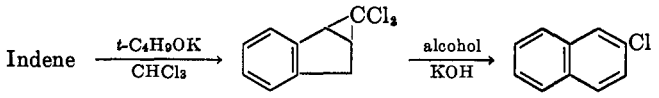
3-Phenylpyridine is obtained in 1 per cent yield from pyrrole and a benzal halide (2, 34, 36).

In 1955 Parham and Reiff (97) treated the sodium salt of indene with chloroform, using indene as the

solvent. In addition to a 65 per cent yield of 2-chloronaphthalene, a blue unstable hydrocarbon, presumably a chloroazulene, was obtained.



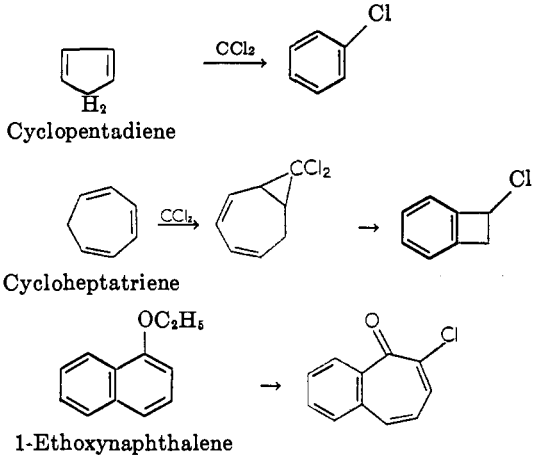
It is important to note that the formation of an azulene establishes the possibility that ring expansion of the six-membered ring has occurred. Proof that the reaction proceeded via addition of dichlorocarbene was obtained by Parham (98), who isolated 1,1-dichloro-1*a*,6*a*-dihydrocyclopropylindene in a nonpolar medium.



Conversion of this adduct to 2-chloronaphthalene occurred rapidly in basic polar media.

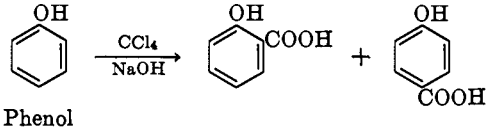
The addition of a dihalocarbene to the indene double bond is inhibited (100) by chlorine, bromine, a carbethoxy group, or a phenyl group, while yields of naphthalenes from indenes with electron-donating groups such as methyl, isopropyl, and ethoxy were comparable to those from indene itself.

More recently dichlorocarbene has been added to cyclopentadiene (29), cycloheptatriene (29), and ethoxynaphthalenes (96), furnishing ring-expansion products:



IV. The Reimer–Tiemann Reaction with Carbon Tetrachloride

Reimer and Tiemann showed in 1876 that when carbon tetrachloride was substituted for chloroform, hydroxy acids could be obtained (112).

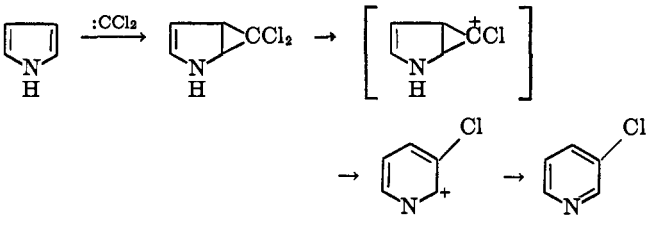


Although this is superficially reminiscent of the Kolbe reaction, fundamental differences must exist, since *o*-nitrophenol, which is unreactive (138) in the Kolbe carboxylation reaction, is reported to furnish the two isomeric carboxylic acids when treated with carbon tetrachloride in alkali (65), the ortho isomer predominating. Adding copper powder, Villani and Lang (132) prepared 2-hydroxy-5-methoxybenzoic acid from hydroquinone monomethyl ether in 74 per cent yield. Rearrangements of abnormal products—trichloromethylcyclohexadienones—have recently been studied (92).

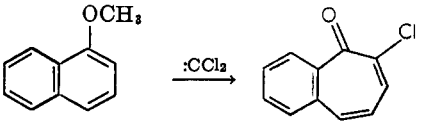
V. Proposed Mechanism for the Reimer–Tiemann Reaction

The work of Hine (67, 68, 69), von Doering (45), Skell (118, 119), Parham (98), and others (79) clearly establishes dihalocarbenes as the electrophilic species in haloform and trichloroacetic acid (5, 29) reactions conducted under alkaline conditions. Direct nucleophilic attack on the haloform by phenoxide carbanion thus appears unlikely (1).

In the absence of a large excess of strongly nucleophilic reagents (phenoxide, hydroxide), dichlorocarbene adds to a double bond. Thus:



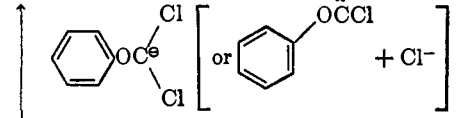
and (96):

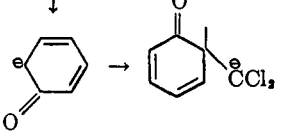


For the reaction in the *presence* of an excess of nucleophilic reagents the following mechanism is suggested:

(A) $CCl_2 \xrightarrow[OH^-]{H_2O} CO + HCOO^- + Cl^-$ (68, 69)

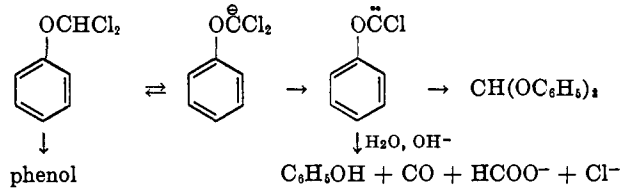
(B) $:CCl_2 + \overset{\ominus}{O}-C_6H_5 \rightarrow$



(C) $:CCl_2 +$  $\rightarrow$

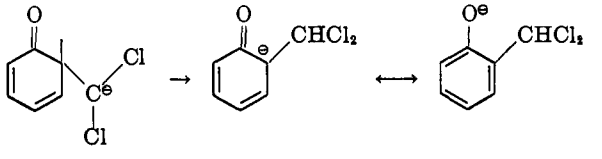
The fate of the primary intermediates appears clear. (*1*) In the first place a large excess of chloroform is needed in the Reimer–Tiemann reaction, since chloroform is consumed rapidly (Case A).

(*2*) In the second case (B) only very small amounts (1–3 per cent) of orthoformic esters are formed, strongly suggesting the rapid decomposition of this intermediate by water and alkali.

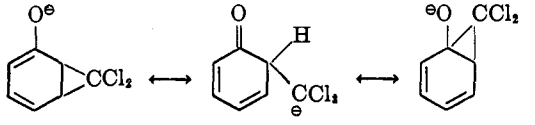


Nucleophilic displacement by phenoxide on dichlorocarbene is here considered possible (70a).

(*3*) (*a*) Finally the nuclear alkylated intermediate may stabilize itself by proton abstraction.

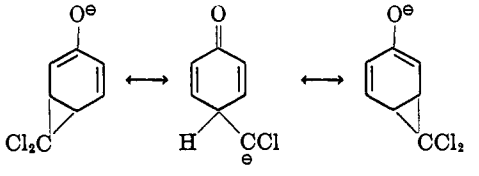


It appears reasonable to assign true dichlorocarbene adduct structures as canonical forms contributing to the stabilization of the intermediate carbanion:



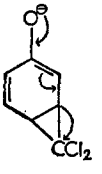
Ib Ia Ic

and

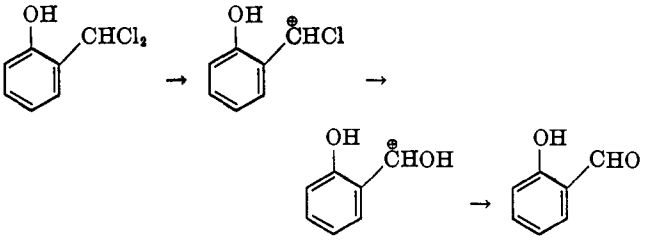


IIb IIa IIc

It is to be noted that opening of the cyclopropane ring of any of the structures (Ib, Ic, IIb, IIc) can only give ortho- and para- but not meta-alkylated products.

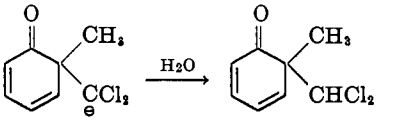


Following proton abstraction, first-order (23, 70) hydrolysis to an aldehyde has established precedent:



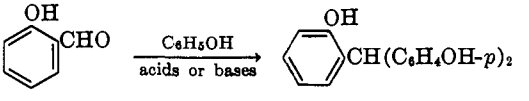
This sequence assigns no role to a "diarylacetal"(5). Acetals of *o*- and *p*-hydroxyaldehydes have been shown by Pauli (101, 102) to be unstable in aqueous medium. The solvolysis of benzal halides in 80 per cent alcohol under alkaline conditions apparently furnishes no acetals (23). Aldehydes can be isolated from the *alkaline* reaction mixture (143).

(*3*) (*b*) The nuclear alkylated intermediate may stabilize itself by proton abstraction from the solvent:



Thus the formation of abnormal products (cyclohexadienones) requires an external proton source, in agreement with the work of Driver (46).

(*4*) The formation of triphenylmethane "resins" must now be ascribed, not to interaction between the phenoxide carbanion with the benzal halide but rather with the hydroxyaldehyde.



Considerable experimental data are available to support the latter contention (37).

VI. Summary

A survey of the Reimer–Tiemann reaction for the formylation of phenols, heterocyclic hydroxy compounds, and certain heterocyclic compounds has been presented. As a reaction conducted in dilute aqueous, alkaline medium and furnishing both ortho and para isomers it is important for the formylation of aromatic compounds. Abnormal products, such as cyclohexadienones and those resulting from ring expansion, may occur in minor or preponderant amounts. The mechanism of the reaction has not been rigorously established, but neither the diarylacetal hypothesis nor a nucleophilic attack on chloroform is in accord with the experimental data. Electrophilic substitution *and* addition by a dihalocarbene agree with known data. The tables show compounds which have been treated under Reimer–Tiemann reaction conditions.

The author wishes to express his thanks to Professor Dr. E. Havinga of the University of Leiden for the

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