

THE KOLBE-SCHMITT REACTION

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I. INTRODUCTION

The Kolbe-Schmitt reaction has been a standard procedure for the preparation of aromatic hydroxy acids for over ninety years. In general, substitution occurs ortho to the phenolic hydroxyl group, but cases of para substitution are also known. Although numerous scattered references appear in the journals, no comprehensive review has hitherto been available. Henecka gives some account of the experimental aspects (98) and Davies briefly mentions the reaction mechanisms proposed prior to 1928 (52).

The purpose of this review is to bring together the many isolated applications of the Kolbe-Schmitt reaction in the form of a general survey. Special emphasis is placed on reaction mechanisms and the various factors which influence the course of the reaction. A tabular summary of the phenols carbonated, together with experimental conditions and yields of hydroxy acids, is presented. An effort has been made to review the literature through January 1956.

II. HISTORICAL

A. KOLBE METHOD

In 1860 Kolbe succeeded in preparing salicylic acid by heating a mixture of phenol and sodium in the presence of carbon dioxide at atmospheric pressure (139, 140, 141). The sodium salicylate formed in this reaction was dissolved in water and the salicylic acid precipitated on acidification. Kolbe wished to show that salicylic acid was monobasic by preparing it from its decomposition products, phenol and carbon dioxide. The successful synthesis in 1860 was a climax to many futile attempts to prepare salicylic acid in this way. Using this same procedure Kolbe also produced *p*-cresotinic acid and *o*-thymotinic acids from *p*-cresol and thymol, respectively (142).

Some years later Kolbe found it necessary to prepare a large amount of salicylic acid. However, on attempting to reproduce the original synthesis, it was found that the yield of salicylic acid varied greatly under seemingly similar reaction conditions. During studies designed to correct this variation in yield, Kolbe found that not only were sodium salicylate and phenol produced in the reaction, but also sodium phenoxide and sodium carbonate. A puzzling feature was that one-half of the initial amount of the phenol was volatilized from the reaction mixture, despite absolutely dry conditions. Kolbe then found that by starting with previously prepared sodium phenoxide a very good yield of salicylic acid was obtained.

With these observations in mind Kolbe recommended a new procedure for the preparation of salicylic acid (137). Sodium phenoxide was prepared by evaporating to dryness an aqueous solution containing equivalent amounts of phenol and sodium hydroxide. The solid phenoxide, which is extremely hygroscopic, was powdered and protected from air until ready for use. The dried sodium phenoxide was heated in an iron retort to 180°C., and carbon dioxide was allowed to pass slowly over the hot salt. The introduction of carbon dioxide caused a large amount of phenol to distil. The temperature was finally raised to 220–250°C., and the reaction was considered complete when no more phenol distilled. In this procedure the yield of salicylic acid never exceeded 50 per cent, since one-half of the starting phenol was lost by volatilization.

B. SCHMITT METHOD

A modification of the Kolbe reaction, in which the carbonation was carried out under pressure and which resulted in greatly improved yields, was described in 1884 by Schmitt, who took out patents covering the preparation of salicylic

and homologous acids (202, 205) and hydroxynaphthoic acids (106, 203). These procedures were subsequently elaborated (204, 207). Thus, for example, dry sodium phenoxide is placed in a closed vessel and heated with carbon dioxide at 120–130° C. for several hours under a pressure of 80 to 94 atm. Under these conditions no phenol is lost and an almost quantitative yield of salicylic acid is obtained. This modified procedure, known as the Kolbe–Schmitt reaction, remains the standard method for the preparation of a wide variety of aromatic hydroxy acids.

C. MARASSE METHOD

A further and by far the most simple modification of the Kolbe–Schmitt reaction was introduced in 1893 by Marasse (159, 160). In this procedure a mixture of the free phenol and excess anhydrous potassium carbonate is carbonated under pressure and at elevated temperature to give the potassium salt of the aromatic hydroxy acid. Acidification gives the free acid in good yield. Recent work indicates that the Marasse modification is fully as general as the Kolbe–Schmitt method and in many cases gives better yields (6, 36, 254). In addition it avoids the time-consuming preparation of the hygroscopic phenoxides.

The excess potassium carbonate acts as an extender and prevents fusion of the mixture with consequent lower yield. Industrially the process would be expensive, since only potassium, rubidium, or cesium carbonates are known to be suitable, the cheaper sodium, magnesium, and calcium carbonates being inert in the reaction. To make the process economically cheaper Marasse later proposed that only one part of potassium carbonate to two parts of phenol be used, with addition of kieselguhr as an extender (1).

D. METHODS INVOLVING THE USE OF SOLVENTS

1. Carbonation in aqueous solutions

While water will inhibit the carbonation of monohydric phenols, the more reactive di- and trihydric phenols—especially where the hydroxyl groups are meta to one another—can be carbonated in alkaline solution. With phenols such as resorcinol, pyrogallol, and phloroglucinol monocarbonation is achieved, in good yield, by heating with fairly concentrated solutions of alkali bicarbonates in an open vessel, usually with passage of carbon dioxide at atmospheric pressure (19, 240, 259).

Thus β -resorcylic acid can be prepared in 60 per cent yield by the carbonation of resorcinol in sodium bicarbonate solution (91, 172). Under similar conditions, but using carbon dioxide under a pressure of 100 atm., *m*-aminophenol may be converted to *p*-aminosalicylic acid in 45 per cent yield (6).

2. Carbonation in organic solvents

The use of toluene as a suspension medium in the carbonation of the metal salts of phloroglucinol and the naphthols with successful results was reported in 1901 (173, 174). Later Brunner employed glycerol as a solvent for carbonations

at atmospheric pressure. The phenol in glycerol solution is heated with alkali bicarbonate in a stream of carbon dioxide at 130–210°C. (32). In general this method does not give as satisfactory results as the Kolbe-Schmitt or Marasse procedures, but it can be used where pressure equipment is not available.

Carbonation of metal aryloxides in dioxane, pyridine, and dialkyl ketones in good yields has been reported (33, 80, 152). The general method is to dissolve the phenol in the solvent, add the calculated amount of solid sodium hydroxide, and, after refluxing, azeotropically distil the water formed. Carbonation can often be effected at atmospheric pressure. Owing to the high cost of organic solvents this method has not been adopted by industry.

3. Carbonation in phenols (*Wacker process*)

Although it was shown in 1923 that sodium or potassium 2-naphthoxide could be satisfactorily carbonated in an excess of 2-naphthol (11), the general applicability of this method was only recognized later by Wacker (248). The procedure is to dissolve one molecular proportion of caustic soda in six molecular proportions of the phenol and distil the excess water at 140°C., adding some xylene if necessary. Carbon dioxide is then passed into the solution at 1 atm. for several hours, and the product is isolated in the usual way. Very pure ortho-carbonated products can be obtained by this method.

E. PRESENT-DAY INDUSTRIAL PROCESSES

The general method of the manufacture of salicylic acid by the carbonation of dry sodium phenoxide with carbon dioxide under pressure is essentially the same in all the major manufacturing countries and has been adequately described (Britain: 256) (Germany: 2, 16, 17, 18, 49, 97) (U. S. A.: 88). The Wacker process is reported to have been used in France (256). Briefly, the process consists in dissolving the phenol in slightly more than one equivalent of hot 50 per cent sodium hydroxide solution. The solution is transferred to a main reactor, consisting of either a vertical closed autoclave equipped with stirrer and baffles or a closed rotary ball mill (67, 68), and is evaporated to dryness by heating at 130°C. under gradual reduction of pressure. Heating is continued until the sodium phenoxide is in a completely dry, powdery form. Carbon dioxide at about 5 atm. pressure is then charged into the reactor, the temperature being held around 100°C.; after absorption of approximately one mole of carbon dioxide, the temperature is raised and held at 150–160°C. for several hours. The carbonation product is cooled and dissolved in water; after treatment with activated charcoal the solution is filtered off. The crude sodium salicylate can be purified by crystallization as the hexahydrate at a temperature below 20°C. (89). Salicylic acid is obtained by acidification of the liquors, and is further purified by sublimation. By-products of the reaction are 2- and 4-hydroxyisophthalic acids, which are found in the "brown dust" residues from the sublimation chambers (120, 124). *p*-Hydroxybenzoic acid is also a by-product of the reaction and is probably lost in the acidification liquors (143).

A similar process is utilized in the manufacture of the three isomeric cresotinic acids and 2-hydroxynaphthoic acid (17). In the case of *p*-hydroxybenzoic acid, potassium hydroxide is substituted for sodium hydroxide, the carbonation of the dry potassium phenoxide being carried out at around 190°C.

Because of the use of *p*-aminosalicylic acid (PAS) in the treatment of human tuberculosis, substantial quantities are now produced by the carbonation of *m*-aminophenol (88, 117; see also Section VI). The general method consists in heating *m*-aminophenol with a solution of potassium bicarbonate under carbon dioxide (30 atm.) at 85°C. in an autoclave for several hours (66, 226, 253). After unchanged material is filtered from the cold solution, addition of hydrochloric acid until the solution is just acid to Congo red precipitates *p*-aminosalicylic acid, which can be further purified by solution in sodium bicarbonate and reprecipitation with acid. Treatment with aqueous sulfurous acid under pressure has also been suggested as a method of separation from the diacid by-product (90). Addition of boric acid to the carbonation mixture has been reported to give increased yields of *p*-aminosalicylic acid (180).

III. FACTORS INFLUENCING THE KOLBE-SCHMITT REACTION

A. EFFECT OF WATER

The use of damp sodium phenoxide or moist carbon dioxide in the salicylic acid synthesis leads to low yields of product; the same is true for the alkali metal salts of other monohydric phenols (39, 137). These salts are hygroscopic and before carbonation are normally dried by heating under reduced pressure. A similar adverse effect of water on yield has been reported in the case of the Marasse method (36, 60). The interesting observation has also been made that carbonation of disodium catechoxide, containing one mole of water, at 134°C. leads to the formation of 2,3-dihydroxybenzoic acid, while perfectly dry starting material yields 2,3-dihydroxyterephthalic acid at 210°C. (39, 209).

Chelation of water molecules with alkali metal ions is of importance in a number of organic reactions (23), and it may well be that in the case of the Kolbe-Schmitt reaction the stronger chelating power of water with the alkali metal aryloxides will prevent the initial addition of carbon dioxide (92, 204). Hydrolysis of the metal salt to the phenol and sodium hydroxide may also occur. Introduction of the carbon dioxide under these conditions will lead only to the formation of sodium bicarbonate, the phenol being unaffected.

As has already been mentioned in this review (Section II), di- and trihydric phenols can be carbonated in aqueous solution in the presence of an alkali metal carbonate such as potassium carbonate, the ease of carbonation varying considerably with the compound employed. Thus catechol, resorcinol, pyrogallol, and phloroglucinol can be carbonated under a stream of carbon dioxide in an open flask, whereas quinol, 2-methylquinol, and *m*-aminophenol must be heated in alkaline solution with carbon dioxide under pressure (19, 144, 164, 240, 258, 259). The greater ease of carbonation of these compounds may arise from lower energies of activation and tautomerization to highly reactive keto forms. Re-

TABLE 1
 Carbonation of phenol

Temperature °C.	Salicylic Acid			<i>p</i> -Hydroxybenzoic Acid			4-Hydroxyisophthalic Acid		
	Na*	K	M	Na	K	M	Na	K	M
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
100	94†	46	49	4	54	51	2	0	0
150	97	54	57	2	44	42	1	2	1
200	96	79	76	2	16	20	2	5	4
250	95	67	63	1	1	1	4	32	36

* The symbols Na and K refer to the carbonation of sodium and potassium phenoxides, and M refers to the Marasse modification.

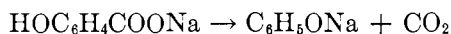
† These values refer to the per cent composition of the total mixed acids isolated. The total overall yields in many of the carbonations amounted to as much as 80 per cent based on the quantity of mixed acids isolated.

sorcinol, for example, is carbonated in the presence of a zinc-copper-chromium oxide catalyst, no alkali being present (135). However, insufficient work has been carried out to justify definite conclusions.

B. EFFECT OF PRESSURE AND TEMPERATURE

At a given temperature, increase of the carbon dioxide pressure above a certain minimum value does not greatly affect the course of the carbonation reaction. However, in some cases an increase in the reaction rate may occur, with a consequent improvement in yield of product for a given reaction time. It has been found (6), for example, that carbonation of sodium or potassium phenoxide under the conditions specified by Kolbe and Schmitt or Marasse is little affected in total yield or relative amounts of the acids formed by variation of the pressure between 80 atm. and 130 atm. or of the time of heating between 4 and 24 hr. (table 1). The rearrangement of sodium 2-hydroxy-1-naphthoate to sodium 2-hydroxy-3-naphthoate during the carbonation of sodium 2-naphthoxide at 145–160°C. is likewise unaffected by increase of pressure up to 45 atm. (231). Increased pressure at high temperatures has been found to lead to disubstitution in the ortho and para positions (128).

The minimal pressure required for quantitative carbonation probably corresponds to the dissociation pressure of the metal aryloxy-carbon dioxide complex at the temperature employed and possibly varies according to the aryloxy used. Davies showed that for the sodium phenoxide-carbon dioxide complex (prepared by heating sodium phenoxide at 105°C. with carbon dioxide under pressure) the dissociation pressure at temperatures above 140°C. lay between 3 and 4 atm. (52). The thermal decomposition of monosodium salicylate in an evacuated system was investigated by plotting the *P*, *T* curve. In this way the equilibrium temperature and pressure for the irreversible reaction



was found to be approximately 150°C. and 74 mm. of mercury, while above 150°C. the reversible reaction

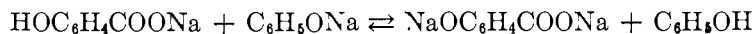


TABLE 2
Carbonation of (A) potassium phenoxide and (B) cesium phenoxide

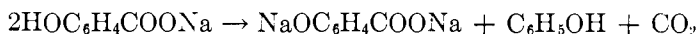
Temperature	Pressure	Total Yield of Mixed Acids	Yield		
			Salicylic acid	<i>p</i> -Hydroxybenzoic acid	
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	
A	140°C.	5 atm.	42	60	40
	210°C.	5 atm.	70	76	24
	240°C.	5 atm.	29	93	5
	180°C.	40 atm.	75	97	3
B	140°C.	5 atm.	31	34	66
	210°C.	40 atm.	63	88	12

The reaction mixture was heated for 4 hr. at the stated temperature, the preheating period being about 15 hr. (254).

TABLE 3
Carbonation of (A) potassium phenoxide and (B) cesium phenoxide at 1 atm. (254)

Temperature	Total Yield of Mixed Acids	Yield		Phenol Distilling Over as Per Cent of Theoretical	
		Salicylic acid	<i>p</i> -Hydroxybenzoic acid		
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>		
A	140°C.	39	59	41	7
	190°C.	43	20	70	—
	210°C.	48	6	94	46
B	140°C.	40	22	78	—
	210°C.	46	7	93	—

was found to occur. At temperatures of 200°C. and above, it has been shown (52) that decomposition of monosodium salicylate proceeds according to the following equation:



The extent to which this occurs at lower temperatures is at present uncertain.

Temperature, in contrast to pressure, greatly influences the reactivity of the aryloxyde as well as the position of substitution. Results illustrating the effect of variation in temperature and alkali metal used are shown in tables 1, 2, and 3.

Although it was early reported that *p*-hydroxybenzoic acid was exclusively obtained by the carbonation of potassium phenoxide (107), recent results (table 3) suggest that ortho substitution occurs initially, with subsequent rearrangement at higher temperatures (128, 254). The rearrangement of sodium 2-hydroxy-1-naphthoate appears to be analogous (231). Thus variation of the products with increasing temperatures may arise either from direct carbonation at different positions in the nucleus or by rearrangement.

C. EFFECT OF ALKALI METAL

The Kolbe-Schmitt reaction is the classical example of a reaction in which the nature of the reaction product is greatly affected by the alkali metal used.

TABLE 4
Effect of the alkali metal on the carbonation product

Compound	Alkali Metal	Temperature	CO ₂ Pressure	Time of Heating	Products	Reference
		°C.	atm.	hours		
Phenol	Li	200	8	18	Salicylic acid (8.7%)	(128)
	Na	200	8	18	Salicylic acid (30.5%)	
	K	200	8	18	Salicylic acid (4.2%) <i>p</i> -Hydroxybenzoic acid (40.6%)	
<i>o</i> - <i>m</i> -Xylenol	Li	170	18	18	3,5-Dimethyl-4-hydroxybenzoic acid (24.2%)	(128)
	Na	170	18	18	3,5-Dimethyl-4-hydroxybenzoic acid (32%)	
	K	170	18	18	3,5-Dimethyl-4-hydroxybenzoic acid (4.8%)	
<i>sym</i> - <i>m</i> -Xylenol	Na	170	10	18	2,4-Dimethyl-6-hydroxybenzoic acid (8.4%)	(128)
	K	170	10	18	2,4-Dimethyl-6-hydroxybenzoic acid (35%) 2,6-Dimethyl-4-hydroxybenzoic acid (1%)	
<i>o</i> -Fluorophenol	Li	160	53	6	3-Fluoro-2-hydroxybenzoic acid (70%)	(75, 76)
	Na	160	53	6	3-Fluoro-2-hydroxybenzoic acid (71%) 3-Fluoro-4-hydroxybenzoic acid (26%)	
	K	160	53	6	3-Fluoro-2-hydroxybenzoic acid (25%)	
					3-Fluoro-4-hydroxybenzoic acid (75%)	

Thus under comparable conditions carbonation of sodium phenoxide will give salicylic acid, while potassium phenoxide yields a mixture of salicylic and *p*-hydroxybenzoic acids (6, 138, 176). Similarly, in the naphthol series sodium 2-naphthoxide yields 2-hydroxy-3-naphthoic acid (the 2-hydroxy-1-naphthoic acid at low temperatures), whereas potassium 2-naphthoxide yields a mixture of 2-hydroxy-3-naphthoic acid and 2-hydroxy-6-naphthoic acid (3, 70). It has been shown that sodium 6-quinolyloxide is not carbonated by being heated for 8 hr. at 175°C. with carbon dioxide under pressure; the potassium derivative gives an almost quantitative yield of 6-hydroxyquinoline-5-carboxylic acid (206). Neither the sodium nor the potassium derivative of carbostyryl could be carbonated under the normal Kolbe-Schmitt or Marasse conditions (86, 129, 244). Some examples of these differences are given in table 4.

The course of a number of organic reactions is greatly altered by varying the alkali metal used. It has been shown that the rate of hydrolysis of ethyl sulfate in 90 per cent aqueous methanol increased through the series NaOH < KOH < N(CH₃)(C₂H₅)₃OH depending on the hydroxide employed (23). Similarly, the ratio of ortho to para products in the Reimer-Tiemann reaction, using 15 *N* alkali solutions, fell through the series NaOH > KOH > CsOH > N(CH₃)(C₂H₅)₃OH. It was suggested that the differences observed were associated with differences in the chelating strengths of the metals used, and it is known that, in the series of alkali and alkaline earth metals, the chelating strengths or stabilizing constants can be correlated with the e^2/r values of the ions (see table 5) (162, 217). Studies of the rearrangement of mono- and dimetalated salicylates suggests that C=O→MO chelation has some influence on the course of this reaction (121, 122, 257). Support for this has been adduced from conductivity measurements of the metal salicylates in acetone, where it was found that the ionization of potassium, rubidium, and cesium salicylates was

TABLE 5
Chelating strengths of metal ions

Ion	Ionic Radius	$\frac{e^2}{r}$	Stability Constant in Case of EDTA*	Ion	Ionic Radius	$\frac{e^2}{r}$	Stability Constant in Case of EDTA
Li ⁺	0.60	1.7	2.8	Cs ⁺	1.67	0.60	No complex
Na ⁺	0.97	1.05	1.7	Ca ²⁺	1.18	3.4	10.6
K ⁺	1.33	0.75	No complex	Sr ²⁺	1.32	3.0	8.6
Rb ⁺	1.47	0.68	No complex	Ba ²⁺	1.53	2.6	7.8

* EDTA = ethylenediaminetetraacetic acid

very much greater than that of lithium and sodium salicylates. On the assumption that a close connection exists between ionization and the chelation effect, it follows that lithium and sodium salicylates, which cannot be rearranged to *p*-hydroxybenzoate, are more strongly chelated than potassium, rubidium, and cesium salicylates, which are readily rearranged on heating.

Some experimental evidence suggests that the carbonation of potassium phenoxide occurs initially at the ortho position, the *p*-hydroxybenzoate arising by subsequent rearrangement (128). It is also known that the carbonation of sodium 2-naphthoxide leads initially to 2-hydroxy-1-naphthoic acid, which rearranges to 2-hydroxy-3-naphthoic acid (231). However, the possibility of intra- or intermolecular carbonation by an activated metal aryloxide-carbon dioxide complex cannot be disregarded (92). A weak chelation effect of $\gg N \rightarrow MO$ has been suggested as a factor adversely affecting the carbonation of carbostyryl (86).

The failure of sodium, magnesium, and calcium carbonates and of sodium bicarbonate in the Marasse carbonation may arise from their insolubility and consequent unreactivity toward phenols, the formation of the metal aryloxide being a necessary prelude to carbonation (36, 254). Potassium bicarbonate and potassium, rubidium, and cesium carbonates, however, readily react with phenols and carbonation then proceeds.

In addition to the differences in chelation strengths of the alkali metals, another factor which possibly influences orientation in the Kolbe-Schmitt reaction is a variation of the electromeric effect with the metal. In dissociating solvents the phenoxy anion is known to have powerful ortho-para-directing properties (126, 127). However, in the solid state or in nondissociating media the polarizability of the metal-oxygen bond will vary with the polarizability of the cation, and this suggests that the electromeric effect will increase through the series $N(C_2H_5)_4O < LiO < NaO < KO < RbO < CsO$ (166). No detailed study of this aspect has been made.

D. EFFECT OF SOLVENT

One of the practical difficulties associated with carbonating metal aryloxides in the solid state lies in the necessity for attaining absolutely anhydrous conditions. A second difficulty lies in the production and maintenance of the dry

TABLE 6
Carbonation in various solvents

Compound	Solvent	Dielectric Constant	Temper- ature	Pres- sure	Acid Product	Yield	Refer- ence
			°C.	atm.			
Sodium phenoxide	Methanol	31.2	140	22	None	—	(128)
	Ethanol	25.8	140	6	None	—	
	1-Butanol	19.2	155	10	Salicylic acid	7.5	
	Glycol	41.2	140	6	None	—	
	Glycerol	56.2	170	10	None	—	
	Xylene (suspension)	2.6	138	1	Salicylic acid	33.5	
Sodium 2-naphthoxide	Dioxane	2.2	260	8	2-Hydroxy-3-naphthoic acid	—	(152)
Sodium 1-naphthoxide	Pyridine	12.5	115	1	1-Hydroxy-2-naphthoic acid	Almost quantitative	(33)
Sodium phenoxide	Diisobutyl ketone	—	150	1	Salicylic acid	18.9	(80)

aryloxide in a finely divided state. Caking during carbonation or inefficient mixing results in low yields and may also lead to superheating, with formation of undesirable by-products.

Use of an inert solvent or suspension medium obviates these difficulties, since azeotropic distillation of part of the solvent will remove water and stirring can be efficiently conducted. Hydrocarbons, for example, can act as solvents for metal phenoxides with long-chain alkyl substituents, but generally the phenoxides are insoluble in this type of solvent and the compound must be carbonated as a finely divided suspension (50, 173, 174, 184, 228).

In addition to the Wacker process, where excess phenol is utilized as solvent, glycerol (32), 1,4-dioxane and 1,3-dioxane (152), pyridine (33), quinoline (33), and dialkyl ketones (80) have been proposed.

Use of a solvent not only facilitates a homogeneous reaction mixture but in a number of cases enables the reaction to be carried out under milder conditions. Sodium 2-naphthoxide, for example, is reported to undergo carbonation readily in dioxane at 50–60°C. and 1 atm. to give 2-hydroxy-1-naphthoic acid (152). Sodium 1-naphthoxide in pyridine at 115°C. under 1 atm. of carbon dioxide gives an almost quantitative yield of 1-hydroxy-2-naphthoic acid (33). Likewise, sodium *p*-benzylphenoxide was found to give 5-benzyl-2-hydroxybenzoic acid in good yield when carbonated in methyl isobutyl ketone solution at 100°C. and 1 atm. (80).

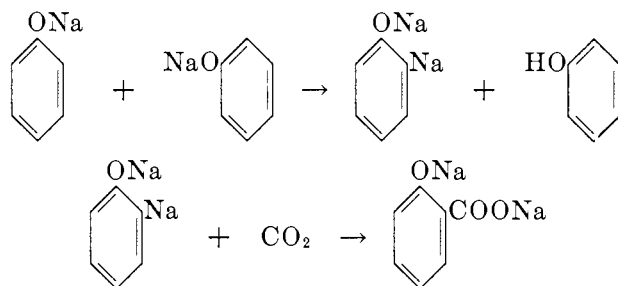
Isemer has pointed out that carbonation proceeds most readily in solvents of low dielectric constant (128). Some supporting experimental results are given in table 6.

IV. PROPOSED REACTION MECHANISMS

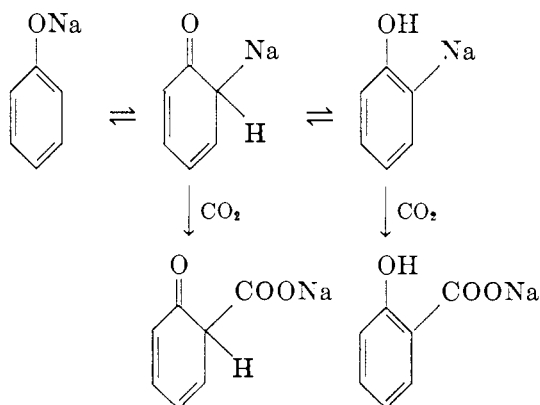
A. METALATION OF AROMATIC NUCLEUS

Kolbe (137) found that for every two moles of sodium phenoxide heated in a stream of carbon dioxide, almost exactly one mole was liberated as phenol, the

other mole being converted into disodium salicylate. To accommodate these facts he postulated ortho metalation of one molecule of sodium phenoxide through sodium-hydrogen interchange with a second molecule, with formation of phenol; the metalated derivative was presumed to react directly with carbon dioxide to yield disodium salicylate.



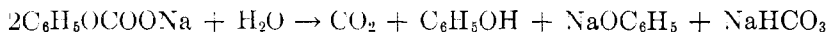
It has been shown that dimetallo derivatives of phenoxides are formed under certain conditions: for example, by refluxing lithium phenoxide with *n*-butyllithium in ether (87). Treatment with carbon dioxide gave salicylic acid in low yield. In the absence of *n*-butyllithium no salicylic acid was obtained. Treatment of 2-naphthol with *n*-butyllithium in boiling benzene followed by subsequent carbonation gave 2-hydroxy-3-naphthoic acid in 7 per cent yield. On the basis of these results and the observations of other workers (82) that some metallic enolates react as true organometallic compounds towards carbon dioxide, it was suggested that at the temperature of the Kolbe-Schmitt reaction the phenoxide tautomerizes to the ortho-metalated forms. These tautomers either react directly with carbon dioxide, as does phenyllithium for example, or react with nontautomerized phenoxide to produce ortho-metalated compounds which then react with carbon dioxide. Further evidence for the existence of di- and trimetalated derivatives of alkali metal phenoxides arises from the presence of salicylic, 2-hydroxyisophthalic, and 2-hydroxyterephthalic acids upon the carbonation of sodium or potassium phenoxide after treatment with *n*-amylsodium in boiling dodecane (166).



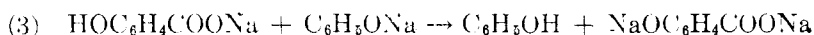
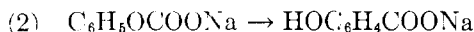
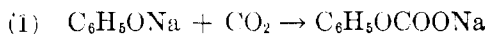
The mechanism involving the formation of ortho-metalated tautomers has however been criticized (92) on the basis that sodium phenoxide at temperatures above 120°C. reacts with an alkyl halide to give substantially the corresponding alkyl phenyl ether. Thus, treatment of sodium phenoxide at 150°C. with *n*-hexyl bromide gives *n*-hexyl phenyl ether in 91 per cent yield. Appreciable quantities of ortho-substituted alkylphenol would be expected to be formed if tautomerism of the type suggested had occurred at this temperature.

B. INTERMEDIATE FORMATION OF METAL ARYL CARBONATE

Although Kolbe suggested in 1860 (141) that large quantities of sodium phenyl carbonate were formed during the reaction of sodium with phenol in the presence of carbon dioxide, he later concluded that sodium bicarbonate was the main by-product (137). Schmitt (204), however, claimed that sodium phenyl carbonate could be prepared by treating perfectly dry sodium phenoxide with dry carbon dioxide. After two to four weeks almost exactly one mole of carbon dioxide was absorbed, increase in volume and development of heat being observed. The substance so formed was a white solid; it was very much less deliquescent than sodium phenoxide and on treatment with water evolved carbon dioxide with formation of phenol, sodium phenoxide, and sodium bicarbonate.

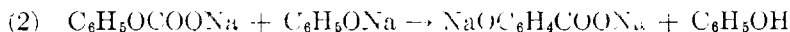
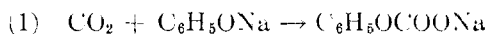


Schmitt criticized Kolbe's suggested mechanism on the basis that although carbon dioxide was absorbed by the sodium phenoxide at temperatures below 100°C., phenol was not liberated until higher temperatures (above 140°C.) were reached. Following an earlier suggestion (9) he postulated initial formation of sodium phenyl carbonate, which subsequently rearranged to give the salt of salicylic acid. The following consecutive reactions were proposed:



Schmitt showed that when his preparation of sodium phenyl carbonate was heated for 1 hr. at 120-130°C. in a sealed tube it was quantitatively converted to monosodium salicylate, and that the latter when heated with a further mole of sodium phenoxide yielded phenol and disodium salicylate.

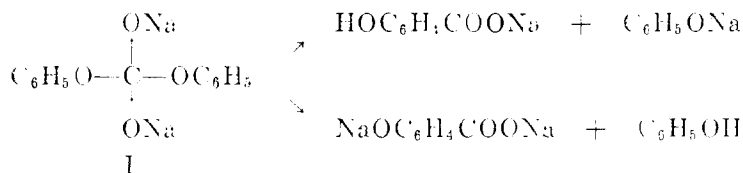
The idea that sodium phenyl carbonate was formed as an intermediate had also been advanced by Hentschel (99), who proposed the following reaction steps:



The similar conversion of potassium phenyl sulfate to potassium *p*-phenolsulfonate observed by Baumann (9) lent support to this idea. Hentschel also showed

that when ethyl phenyl carbonate was heated with dry sodium phenoxide, monosodium salicylate and phenetole were the only products. Similarly, sodium salicylate and anisole were obtained quantitatively from diphenyl carbonate and sodium methoxide.

It was later suggested (165) that I was an intermediate in the Kolbe-Schmitt reaction, being formed either by reaction of sodium phenoxide with the sodium phenyl carbonate or by reaction of two moles of sodium phenoxide with carbon dioxide directly. Breakdown of I may occur by either of the routes shown. No very convincing evidence was advanced to support this theory.

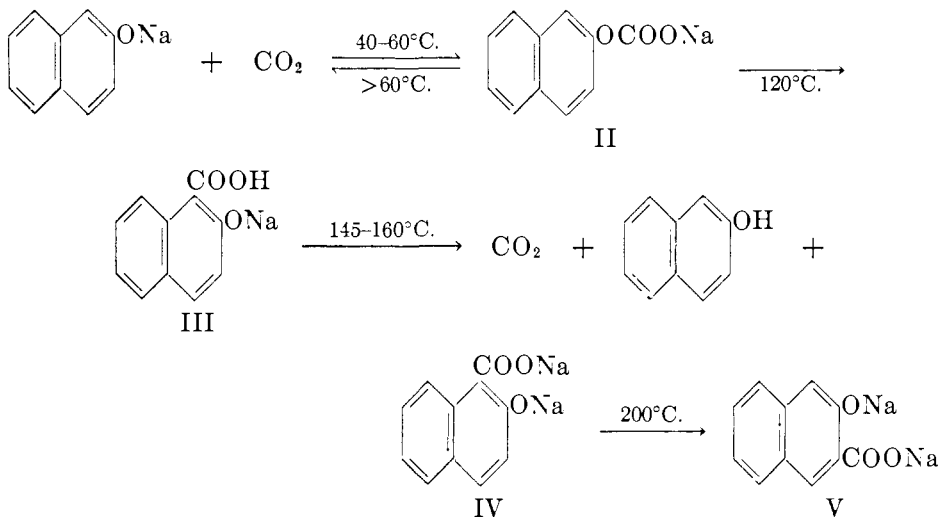


Suiter (234) found that on heating diphenyl carbonate with two moles of sodium hydroxide, sodium carbonate and phenol were formed; with one mole of sodium hydroxide, phenol and phenyl sodium carbonate were formed. Approximately 60 per cent of the latter underwent immediate decomposition, at 160°C. and 1 atm., into carbon dioxide and sodium phenoxide, and 40 per cent rearranged to monosodium salicylate. These experiments were claimed to prove that sodium phenyl carbonate could act as an intermediate product in the Kolbe-Schmitt reaction (242).

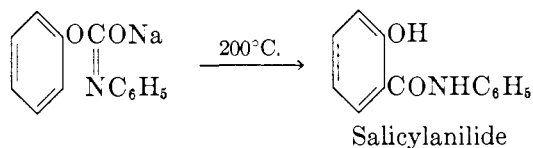
Davies (52), by measurement of the carbon dioxide equilibrium pressure during the salicylic acid synthesis, concluded that two, not previously recognized "ester salts" were formed. At about 85°C. the "ester salt I" was formed from sodium phenoxide and carbon dioxide, which at 120–140°C. underwent an intramolecular conversion to "ester salt II," which rearranged to form sodium salicylate without any decrease in pressure occurring. In addition the P, T curve showed an inflexion at 190° and 4.15 atm., which Davies regarded as the quintuple point of the following five phases: monosodium salicylate, disodium salicylate, sodium phenoxide, phenol (molten phase), and carbon dioxide (gaseous phase). Later Sinkow showed (232) that the "ester salts I and II" were identical, and that the results observed by Davies and earlier workers (10) obeyed the Nernst and Clausius-Clapeyron equations, indicating a heterogeneous equilibrium. It was further suggested that the formation of *p*-hydroxybenzoate during the reaction would also complicate the interpretation of the results (143).

Later workers (231) examined the carbonation of dry sodium 2-naphthoxide and found that at low temperatures (40–60°C.) a reaction occurred; the product, which they considered to be sodium β -naphthyl carbonate (II), dissociated at higher temperatures into its components. At 120°C. under pressure with carbon dioxide, II rearranged to give 1-carboxy-2-sodium naphthoxide (III). Interaction of this product with itself at 145–160°C. led to the formation of disodium 2-oxo-1-naphthoate (IV), 2-naphthol, and carbon dioxide. When the reaction

mixture was heated at 200°C. the rearrangement to disodium 2-oxy-3-naphthoate (V) occurred. It was claimed, without experimental details, that the carbonation product (III) would readily absorb dry ammonia, thus confirming its structure. The intermediate carbonate (II) was considered to decompose to give "active carbon dioxide," which then carbonated the sodium naphthoxide (cf. Section IV, C). A somewhat similar mechanism for the reaction was advanced by Gershzon (85), who claimed to have prepared $C_6H_5C(=NC_6H_5)ONa$ by treating the phenyl ester of phenylcarbamic acid with sodium in boiling xylene. The



sodium compound in the reaction mixture was heated in a sealed tube at 200°C. for 1 hr. and yielded about 20 per cent of salicylanilide. The 1-naphthyl and 2-naphthyl esters under similar treatment yielded the corresponding hydroxy-



naphthoic anilides. It was claimed that these experiments proved the intermediate formation of metal aryl carbonates in the Kolbe-Schmitt reaction; this claim was later shown to be without basis by Chelintsev, who found that the products arising by treatment of the phenyl ester of phenylcarbamic acid with sodium were diphenylurea and triphenyl isocyanurate (40). The triphenyl isocyanurate suggested the presence of phenyl isocyanate in the reaction mixture. It was shown that salicylanilide was formed by heating phenyl isocyanate with sodium phenoxide. Gershzon's "proof" of the mechanism is therefore invalid.

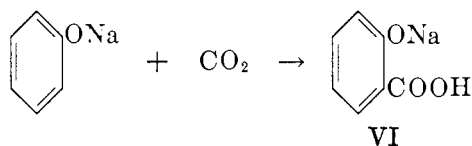
The theory of intermediate formation of a metal aryl carbonate is not supported by the observations of some recent workers (92), who consider that the initial reaction of carbon dioxide with the metal aryloxyde at low temperatures

involves weak chelation of the gas with the metal to give an unstable complex. Thus the ready dissociation of the complex into its components under a vacuum or at atmospheric pressure on heating would be explained. The evolution of carbon dioxide on treatment of the complex with dry acetone (165) and on treatment with water (204) probably arises from the stronger chelating power of these solvents, leading to displacement of carbon dioxide; in the case of water subsequent reaction occurs. Acetone has been shown to form an equimolecular complex with sodium phenoxide (221), the acetone being removable under vacuum; similarly, phenol will chelate with sodium phenoxide (84).

The sodium phenoxide-carbon dioxide complex was shown to give rise to a carbonyl absorption band at 1684 cm.^{-1} in the infrared, whereas sodium methyl carbonate, a stable recrystallizable solid, gave rise to carbonyl absorption at 1630 cm.^{-1} . Similarly, the complex prepared from carbon dioxide and sodium 2-cresoxide possesses a carbonyl absorption at around 1670 cm.^{-1} (154). Davies (52) showed the dissociation pressure of this complex to be around 4 atm. between 120°C. and 160°C. ; hence it could well be the true intermediate in the carbonation process.

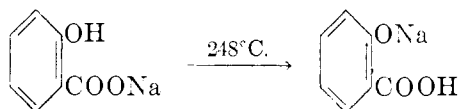
C. DIRECT NUCLEAR CARBONATION

In 1904 it was shown (155) that the compound prepared from sodium phenoxide and carbon dioxide by Schmitt would dissociate into its components at 85°C. , the vapor pressure then being about 1 atm. These workers considered that such an intermediate could not exist under the Kolbe conditions of carbonation and was also unlikely under the Schmitt conditions. Carbonation must therefore occur by direct nuclear substitution. A carbonate intermediate was,



however, not ruled out for the carbonation of other compounds such as sodium 8-quinolyl oxide (208). Subsequently Tijnstra claimed to have proved this theory by means of the following experiments (241): (1) Only a slight increase in weight could be detected after heating sodium phenoxide at 110°C. with carbon dioxide at atmospheric pressure, indicating that no reaction had occurred. (2) Heating the carbonation product—believed to be sodium salicyloxyde (VI)—with methyl iodide yielded methyl salicylate. Since *o*-methoxybenzoic acid readily rearranges to methyl salicylate under basic conditions this test was inconclusive. (3) The dissociation pressure of sodium salicyloxyde at 180°C. after one day was found to be approximately 1 atm. Sodium salicylate at 180°C. had a dissociation pressure of only 534 mm. after two days. The difference was shown by introducing a small amount of the carbonation product into paraffin oil at 180°C. ; a turbulent evolution of gas occurred. Sodium salicylate yielded no gas under similar conditions. (4) The carbonation product was found to

absorb dry ammonia, whereas sodium salicylate did not. The carbonation product after being heated for 20 hr. with water and then evaporated to dryness would still absorb ammonia. Sodium salicylate heated at 248°C. for 2.5 hr. and washed with ether (traces of phenol) also absorbed ammonia. It was considered that the rearrangement shown below had taken place:



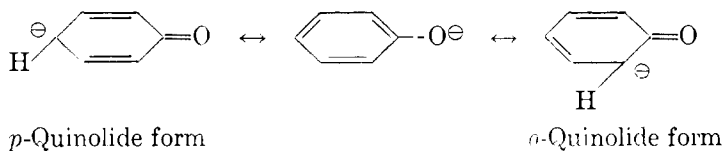
Tijmstra's evidence can be criticized on the grounds that the product prepared by carbonating sodium phenoxide with carbon dioxide under pressure always contains small amounts of phenol and sodium bicarbonate when moisture is not rigorously excluded from the autoclave (92). The presence of these by-products would explain the observations listed under 3 and 4 above. Furthermore, monosodium salicylate heated at 220°C. and above is converted into a mixture of disodium salicylate, phenol, and carbon dioxide (123, 176). Tijmstra's conclusions are therefore doubtful.

Similar doubtful conclusions have been reached in the case of the carbonation of sodium 2-naphthoxide (219), where direct nuclear carbonation is postulated. The sodium hydroxynaphthoate first formed is considered to decompose into its components at higher temperatures (280°C.) with recarbonation of the nucleus to give sodium 2-hydroxy-3-naphthoate, the latter then undergoing reaction with a further molecule of sodium 2-naphthoxide to yield disodium 2-oxy-3-naphthoate and free 2-naphthol. This mechanism appears unlikely, since it has been shown that quantitative conversion of disodium 2-oxy-1-naphthoate to the 2-oxy-3-naphthoate occurs at 300°C. (113).

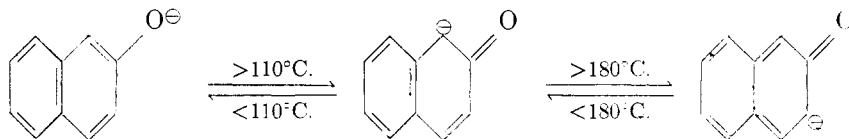
Tijmstra's formulation of the carbonation product in the phenol series as sodium salicyloxyde (VI) has been shown (92) to be untenable on the basis of its infrared spectrum. This, however, does not rule out the possibility that the original hypothesis of direct nuclear carbonation may represent the first step in the reaction, and that subsequent interchange of hydrogen and sodium ions (or atoms) occurs, giving sodium salicylate as the final product.

D. TAUTOMERIC REARRANGEMENT

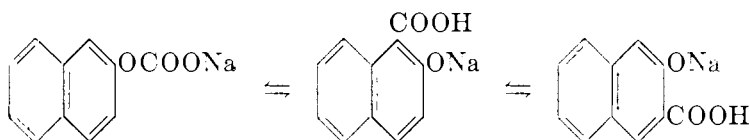
By analogy with the reaction of carbon dioxide with the metal enolates of some ketones (29) to give β -keto acids, Hückel suggested (118) that the Kolbe-Schmitt reaction proceeded by the addition of carbon dioxide to the mesomeric phenoxy or naphthoxy anion, the predominance of the mesomeric form being governed by the alkali metal used.



This idea has also been advanced to explain the different carbonation products of sodium 2-naphthoxide at different temperatures (132). It is considered that, with increasing temperatures, one of the resonance forms of the naphthoxide ion becomes more predominant than the others, thus giving rise to the different products.



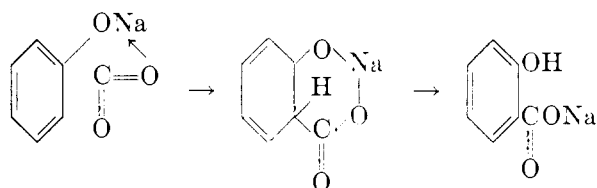
The postulated products for carbon dioxide addition are:



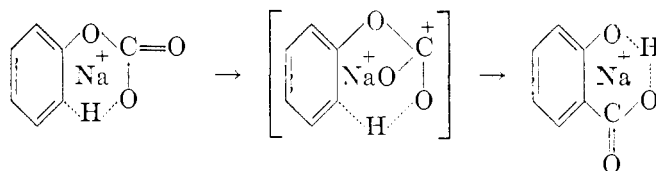
No direct experimental evidence is at present available on which to judge the correctness of these views.

E. CHELATE FORMATION AND ELECTROPHILIC SUBSTITUTION

Johnson (131) found that benzylmagnesium chloride often reacted with various compounds to give abnormally the *o*-tolyl derivatives, and by analogy suggested that the Kolbe-Schmitt reaction proceeded by the mechanism illustrated in the sequence below. The primary addition product was considered to be bound by a coordinate linkage, the activated molecule then substituting at

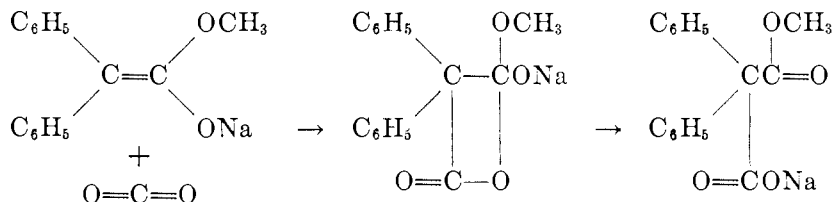


the ortho position with stabilization of the transition stage by ring formation. Luttringhaus (158), on the basis of his results on rearrangement during the fission of ethers by means of alkali metals, tentatively suggested that during the Reimer-Tiemann aldehyde synthesis and the Kolbe-Schmitt salicylic acid synthesis a cyclic stage was involved, leading to ortho substitution, viz:



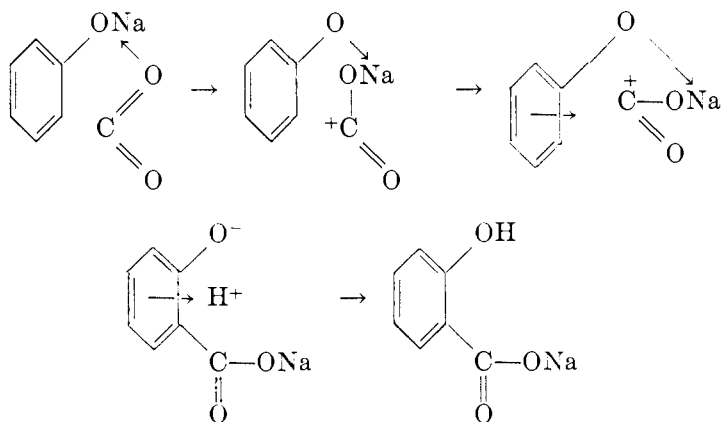
In the case of potassium phenoxide under these conditions, owing to the limited degree of chemical stability and also to the greater ionic volume of potassium,

p-hydroxybenzoate will result. A cyclic intermediate has also been postulated by other workers (198) during the carbonation of ester enolates. This reaction mechanism, shown below, involves the formation of a four-membered ring intermediate.



Now it is known that phenol will undergo carbonation under Kolbe-Schmitt conditions only in the form of the alkali metal phenoxide (135). In the Marasse modification of the reaction (see Section II, C above), where the free phenol is heated with anhydrous carbonate and carbon dioxide under pressure, it has been shown that phenoxide formation is a necessary prelude to reaction (254). It therefore seems likely that this type of carbonation involves electrophilic attack on the ortho carbon atom (220). Presumably a similar process can operate when carbonation is carried out in phenol solution; here one of the phenol molecules of the sodium phenoxide-phenol solvate would be displaced by a molecule of carbon dioxide, with subsequent attack on the ortho position.

A mechanism based on the preliminary association of sodium phenoxide with carbon dioxide under pressure to form a complex, and involving intramolecular reaction with displacement of the ortho hydrogen by electrophilic attack has been suggested (92). If the transition stage involves a π -complex, and the oxygen atom in solid sodium phenoxide is coplanar with the benzene ring so that its "lone pair" electrons can take part in a molecular π -electron orbital, then the proton displaced onto the π -electron system would migrate to the phenolic oxygen (55).



V. APPLICATION OF THE KOLBE-SCHMITT REACTION

A. AROMATIC SERIES

In general, as with other electrophilic reactions, the presence of alkyl groups in the aromatic nucleus promotes ortho carbonation in phenols with high yields of product. The effect is most marked with para-substituted and less so for ortho-substituted alkylphenols. The reactivity, however, is modified by a steric hindrance factor. Where the hydroxyl is flanked by two ortho alkyl substituents only a low yield of the para-carbonated compound is obtained. Similarly, with two alkyl substituents both in the meta positions, only low yields of the ortho-carbonated product are realized. These results are exemplified in the case of the xylenols (6, 36, 179, 254). Where both the ortho and the para positions carry alkyl substituents no carbonation occurs (128). Phenyl groups ortho or para to the hydroxyl promote high yields of the ortho-carbonated product, while para-substituted aryl groups have a deactivating effect with consequent reduced yields of the acid. Some differences arising from the use of different alkali metal derivatives of the alkylphenols have already been given in Section III, C.

For other substituents in the phenolic nucleus it can be stated that, in general, electron-donating substituents facilitate the carbonation reaction, while electron-withdrawing substituents retard or inhibit carbonation. Thus the presence of amino, methoxyl, or additional hydroxyl groups usually enables the reaction to be carried out at lower temperatures and with increased yields of products. The halogen-substituted phenols can be carbonated under both Kolbe-Schmitt and Marasse conditions, the *o*-, *m*-, and *p*-fluoro-, chloro-, and bromophenols giving satisfactory yields, whereas low yields are obtained from the *o*-, *m*-, and *p*-iodophenols (6, 254). In the case of *o*-fluorophenols ortho and para carbonation occurs, the relative amounts depending on the alkali metal used (Section III, C) (76).

In contrast, electron-withdrawing substituents such as nitro, nitrile, and carboxylate ion retard carbonation. Thus *m*-nitrophenol gives only a 19 per cent yield of acid under Marasse conditions (254), while the *o*- and *p*-nitro- and *o*-cyanophenols are inert (128, 129). Carboxylate ions and acyl groups have a lower deactivating effect on the ring, however, and can often be carbonated at higher temperatures.

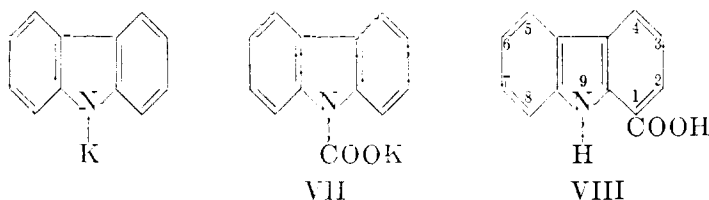
B. HETEROCYCLIC SERIES

Carbonation of the heterocyclic aromatic nucleus has been less extensively studied than carbonation of the carbocyclic aromatic series, and the number of successful carbonations reported in the literature is relatively small.

In the pyridine series 2-, 3-, and 4-hydroxypyridines have been carbonated under Kolbe-Schmitt or Marasse conditions. In the former instance para-substitution occurs exclusively (6, 244), while the second compound gives the ortho or para acid depending on the reaction conditions; the third compound gives only the ortho mono- or dicarboxylic acid (6, 21, 22).

Carbonation of the heterocyclic nucleus of hydroxyquinolines or hydroxyisoquinolines has not yet been reported. However, 6-hydroxy- and 8-hydroxyquinoline can be successfully carbonated in the carbocyclic aromatic nucleus (206, 208). The known lower reactivity of quinoline compounds, as well as reduced mobility of the metal through chelation, has been suggested as a reason for the failure of carbonation experiments (86).

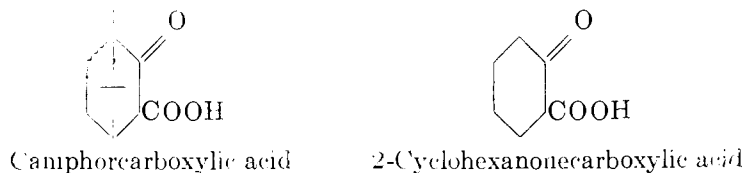
Pyrrole is well known to behave analogously to phenol and it was early found that 2-pyrrolecarboxylic acid was formed by heating pyrrole with aqueous ammonium carbonate in a sealed tube (46). The same product admixed with the 3-carboxylic acid was also obtained by heating potassium pyrrole in a stream of carbon dioxide at 200–220°C. The potassium derivatives of 2- and 3-methylpyrrole could similarly be carbonated (41, 42, 43, 47, 48). Potassium carbazole carbonated by a similar process was initially thought to give the carbamic acid (VII), but the product was later shown to be 1-carbazolecarboxylic acid (VIII), identical with the substance obtained by treating the Grignard reagent with carbon dioxide (26, 45).



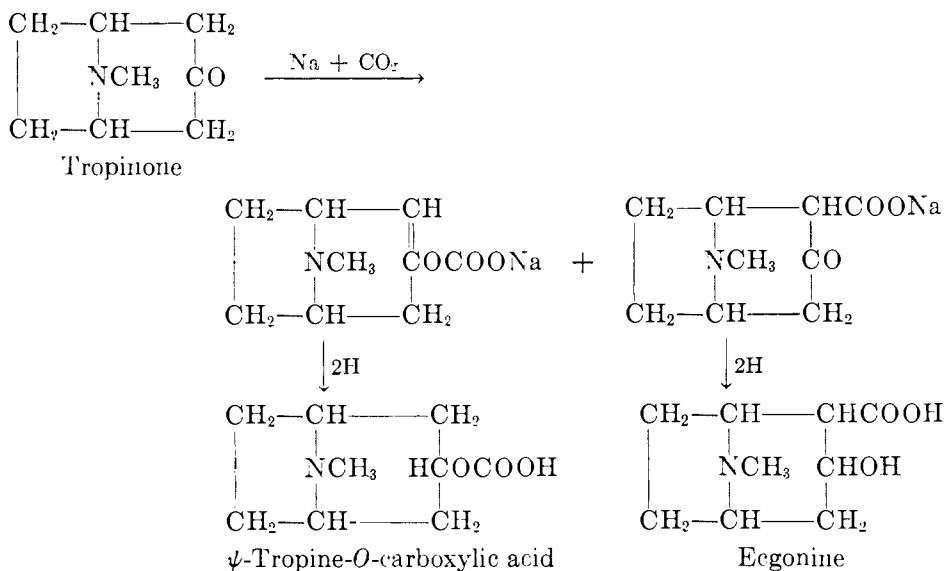
A number of other miscellaneous hydroxy heterocyclic aromatic compounds have been carbonated by the Kolbe-Schmitt reaction, including 2-hydroxycarbazole and tetrahydro-7-hydroxynaphthylcarbazole, but no systematic study has been carried out.

C. OTHER COMPOUNDS

The carbonation of the metal enolates of cyclic and aliphatic ketones bears some analogy to that of metal aryloxides, and a postulated mechanism for the carbon dioxide addition has already been referred to (page 600). The earliest experiments along these lines were the preparation of camphorcarboxylic and cyclohexanonecarboxylic acids by treatment of the ketone with sodium or sodium amide and carbon dioxide (8, 24, 25, 29, 30, 146).

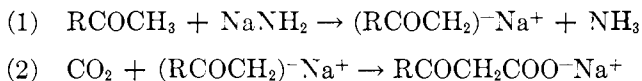


A similar procedure was used to prepare ecgonine and ψ -tropine-*O*-carboxylic acid from tropinone (260).



A more extensive investigation of the possibility of carbonating cyclohexanone and its derivatives was carried out in 1910, and the successful preparation of 2-cyclohexanonecarboxylic acid, 1-methylcyclohexan-2-one-3-carboxylic acid, *dl*- and *l*-1-methylcyclohexan-3-one-4-carboxylic acid, 1-methylcyclohexan-4-one-3-carboxylic acid, and *d*-isomethonedicarboxylic acid was reported (83). A recent attempt to carbonate tropolone was unsuccessful (51, 86).

An interesting extension of the carbonation reaction to the preparation of 2-ketocarboxylic acids from dialkyl or alkyl aryl ketones has been recently reported (153). The sodium enolate was prepared by treatment of the ketone with sodium amide in liquid ammonia. A two-step mechanism involving addition of carbon dioxide to the ketonic anion was suggested:



In general, carbonations of the type discussed are favored by anhydrous conditions and low temperatures, ether and ligroin being the preferred solvents.

VI. TABULATION OF COMPOUNDS CARBONATED

Tables 7 to 12 present data on the following classes of compounds which have been carbonated: mononuclear monohydric phenols, mononuclear polyhydric phenols, dinuclear phenols, polynuclear phenols, heterocycles, and ketones.

The information quoted in these tables is taken from the initial reference given; subsequent references give alternative methods of preparation or additional information. The range of compounds included is as extensive as possible, but no claim is made that the tables are complete. A number of Kolbe-Schmitt

TABLE 7
Mononuclear monohydric phenols

Phenol	Conditions				Products	Yield	References
	Metal or Marasse	Temperature	CO ₂ pressure	Time of heating			
		°C.	atm.	hours		per cent	
2-Methyl.....	Na	200	40	6	3-Methyl-2-hydroxybenzoic acid	70	(254, 6, 17, 64, 65, 112, 125, 134, 248)
	M	200	40	4	3-Methyl-2-hydroxybenzoic acid 5-Methyl-4-hydroxyisophthalic acid	56 14	(254, 6, 32)
3-Methyl.....	Na	125	100	8	4-Methyl-2-hydroxybenzoic acid	70	(6, 15, 17, 125)
	M	175	100	4	4-Methyl-2-hydroxybenzoic acid	85	(6)
4-Methyl.....	Na	200	40	6	5-Methyl-2-hydroxybenzoic acid	85	(254, 6, 17, 125, 142, 197)
	M	200	40	4	5-Methyl-2-hydroxybenzoic acid	91	(254, 6, 36)
3-Trifluoromethyl.....	M	220	20	240	3-Trifluoromethyl-2-hydroxybenzoic acid	88	(94)
2-Ethyl.....	Na	—	1	—	3-Ethyl-2-hydroxybenzoic acid	—	(12)
3-Ethyl.....	M	175	100	4	4-Ethyl-2-hydroxybenzoic acid	83	(6)
4-Ethyl.....	Na	—	1	—	5-Ethyl-2-hydroxybenzoic acid	—	(12)
2- <i>n</i> -Propyl.....	Na	140	1	—	3- <i>n</i> -Propyl-2-hydroxybenzoic acid	—	(236)
4- <i>n</i> -Propyl.....	Na	140	1	—	5- <i>n</i> -Propyl-2-hydroxybenzoic acid	—	(236)
2-Isopropyl.....	Na	150	1	—	3-Isopropyl-2-hydroxybenzoic acid	—	(79)
4-Isopropyl.....	Na	145	1	8	5-Isopropyl-2-hydroxybenzoic acid	—	(181)
2- <i>n</i> -Butyl.....	Na	—	—	—	3- <i>n</i> -Butyl-2-hydroxybenzoic acid	—	(254)
					3- <i>n</i> -Butyl-2-hydroxyisophthalic acid	—	
4-Isobutyl.....	Na	160	—	4	5-Isobutyl-2-hydroxybenzoic acid	93	(56)
4- <i>tert</i> -Butyl.....	Na	150	100	8	5- <i>tert</i> -Butyl-2-hydroxybenzoic acid	74	(6)
	M	200	100	4	5- <i>tert</i> -Butyl-2-hydroxybenzoic acid	90	(6)
2- <i>n</i> -Amyl.....	Na	—	—	—	3- <i>n</i> -Amyl-2-hydroxybenzoic acid	—	(254)
4- <i>n</i> -Amyl.....	Na	—	—	—	5- <i>n</i> -Amyl-2-hydroxybenzoic acid	—	(254)
2-Allyl*.....	Na	140	20	—	3-Allyl-2-hydroxybenzoic acid	—	(74)
4-(2-Butenyl)*.....	Na	140	20	—	4-(2-Butenyl)-2-hydroxybenzoic acid	—	(74)
2-Methoxy.....	M	200	100	4	3-Methoxy-2-hydroxybenzoic acid	47	(6, 185)
3-Methoxy.....	M	200	100	4	4-Methoxy-2-hydroxybenzoic acid	61	(6)
4-Methoxy.....	M	150	100	4	5-Methoxy-2-hydroxybenzoic acid	90	(6)
2-Ethoxy.....	M	185	8	—	3-Ethoxy-2-hydroxybenzoic acid	40	(185)
4-Propionyl.....	M	175	100	4	5-Propionyl-2-hydroxybenzoic acid	25	(6)
2-Carboxy.....	Na (di)	400	1	24	4-Hydroxyisophthalic acid	—	(177, 178)
					6-Hydroxytrimeric acid	—	
2-Carbomethoxy.....	Na	150	—	24	2-Hydroxy-3-carbomethoxybenzoic acid	—	(209) (110)
3-Carbomethoxy.....	Na	170	—	—	2-Hydroxy-4-carbomethoxybenzoic acid	—	(209, 110)
4-Carbomethoxy.....	Na	170	—	—	2-Hydroxy-5-carbomethoxybenzoic acid	—	(209, 110)

4-Carboxy	Na	170	--	--	2-Hydroxy-5-carboxybenzoic acid	--	(209, 110)
2-Fluoro	Na	160	53	6	3-Fluoro-2-hydroxybenzoic acid	68	(76, 35)
	K	160	53	6	3-Fluoro-4-hydroxybenzoic acid	29	
	Li	160	53	6	3-Fluoro-2-hydroxybenzoic acid	25	(76, 6)
	M	175	100	8	3-Fluoro-4-hydroxybenzoic acid	75	
3-Fluoro	Na	175	100	8	3-Fluoro-2-hydroxybenzoic acid	70	(75)
	M	175	100	4	4-Fluoro-2-hydroxybenzoic acid	59	(6)
4-Fluoro	Na	175	100	8	4-Fluoro-2-hydroxybenzoic acid	72	(6)
	M	225	100	4	5-Fluoro-2-hydroxybenzoic acid	44	(6)
2-Chloro	Na	150	100	8	5-Fluoro-2-hydroxybenzoic acid	77	(6)
	M	175	100	4	3-Chloro-2-hydroxybenzoic acid	64	(6, 245)
3-Chloro	Na	175	100	8	3-Chloro-2-hydroxybenzoic acid	72	(6, 254)
	M	175	100	4	4-Chloro-2-hydroxybenzoic acid	68	(6, 245)
4-Chloro	Na	150	100	8	4-Chloro-2-hydroxybenzoic acid	68	(6, 254)
	M	175	100	4	5-Chloro-2-hydroxybenzoic acid	69	(6, 245)
2-Bromo	Na	175	100	8	5-Chloro-2-hydroxybenzoic acid	83	(6, 254)
	M	175	100	4	3-Bromo-2-hydroxybenzoic acid	64	(6)
3-Bromo	Na	175	100	8	3-Bromo-2-hydroxybenzoic acid	64	(6)
	M	175	100	4	4-Bromo-2-hydroxybenzoic acid	80	(6)
4-Bromo	Na	175	100	8	4-Bromo-2-hydroxybenzoic acid	51	(6)
	M	175	100	4	5-Bromo-2-hydroxybenzoic acid	5	(6)
2-Iodo	M	125	100	8	5-Bromo-2-hydroxybenzoic acid	79	(6, 254)
3-Iodo	M	125	100	8	3-Iodo-2-hydroxybenzoic acid	31	(6)
4-Iodo	M	125	100	8	4-Iodo-2-hydroxybenzoic acid	35	(6)
2-Amino	M	220	50	14	5-Iodo-2-hydroxybenzoic acid	6	(6)
3-Amino†	KHCO ₂	90	--	6	3-Amino-2-hydroxybenzoic acid	5	(253)
					4-Amino-2-hydroxybenzoic acid (PAS)	80	(66, 5, 14, 57, 59, 77, 101, 102, 103, 119, 133, 149, 163, 186, 187, 188, 189, 190, 226, 237, 238, 239, 249, 250, 253, 255)
4-Amino	M	200	50	8	5-Amino-2-hydroxybenzoic acid	76	(253)
3-Methylamino†	KHCO ₂	96	3	90	4-Methylamino-2-hydroxybenzoic acid	20	(58)
3-Diethylamino	M	175	100	8	4-Diethylamino-2-hydroxybenzoic acid	51	(6)
3-Allylamino†	KHCO ₂	96	3	90	4-Allylamino-2-hydroxybenzoic acid	20	(58)
2-Acetamido	M	175	100	4	3-Acetamido-2-hydroxybenzoic acid	11	(6)
3-Acetamido	M	175	100	4	4-Acetamido-2-hydroxybenzoic acid	75	(6)
4-Acetamido	M	200	100	8	5-Acetamido-2-hydroxybenzoic acid	71	(6)
2-Nitro	M	210	40	4	No carbonation	0	(254)
3-Nitro	M	210	40	4	4-Nitro-2-hydroxybenzoic acid	19	(254)
4-Nitro	M	210	40	4	No carbonation	0	(254)

* Naptha or dioxane used as solvent.

† Water used as solvent.

TABLE 7—Concluded

Phenol	Conditions				Products	Yield	References
	Metal or Marasse	Tempera-	CO ₂	Time of			
		ture	pressure	heating			
		°C.	atm.	hours		per cent	
2-Cyano	M	210	40	4	No carbonation	0	(254)
2,4-Dimethyl	Na	240	35	40	3,5-Dimethyl-2-hydroxybenzoic acid	17	(179)
2,5-Dimethyl	Na	240	35	40	3,6-Dimethyl-2-hydroxybenzoic acid	72	(179, 175)
	M	175	100	4	3,6-Dimethyl-2-hydroxybenzoic acid	25	(6)
2,6-Dimethyl	Na	200	40	6	3,5-Dimethyl-4-hydroxybenzoic acid	37	(254)
3,4-Dimethyl	Na	200	40	6	4,5-Dimethyl-2-hydroxybenzoic acid	89	(254, 179)
	M	200	40	4	4,5-Dimethyl-2-hydroxybenzoic acid	93	(254, 6)
3,5-Dimethyl	Na	200	40	6	4,6-Dimethyl-2-hydroxybenzoic acid	30	(254, 179, 81)
	M	200	40	6	4,6-Dimethyl-2-hydroxybenzoic acid	93	(254, 6)
2-Methyl-4-isopropyl	Na	—	1	—	3-Methyl-5-isopropyl-2-hydroxybenzoic acid	—	(130, 142)
2-Methyl-5-isopropyl	Na	—	1	—	3-Methyl-6-isopropyl-2-hydroxybenzoic acid	—	(157)
5-Methyl-2-isopropyl†	Na	140	1	5	6-Methyl-3-isopropyl-2-hydroxybenzoic acid	Quantitative	(235)
2-Methoxy-4-methyl	M	200	100	4	3-Methoxy-5-methyl-2-hydroxybenzoic acid	69	(6)
3,5-Dimethoxy	Na	—	—	—	4,6-Dimethoxy-2-hydroxybenzoic acid	—	(105)
2-Bromo-4- <i>tert</i> -butyl	Na	200	100	8	3-Bromo-5- <i>tert</i> -butyl-2-hydroxybenzoic acid	58	(6)
	M	175	100	4	3-Bromo-5- <i>tert</i> -butyl-2-hydroxybenzoic acid	46	(6)
4-Chloro-2-allyl*	Na	140	20	—	5-Chloro-3-allyl-2-hydroxybenzoic acid	—	(74)
5-Chloro-2-allyl*	Na	140	20	—	6-Chloro-3-allyl-2-hydroxybenzoic acid	—	(74)
4-Chloro-3-propenyl*	Na	110	20	—	5-Chloro-3-propenyl-2-hydroxybenzoic acid	—	(74)
2,4-Dichloro	Na	200	100	8	3,5-Dichloro-2-hydroxybenzoic acid	59	(6)
	M	200	100	4	3,5-Dichloro-2-hydroxybenzoic acid	45	(6)
2,4-Dibromo	M	175	100	4	3,5-Dibromo-2-hydroxybenzoic acid	38	(6)
2-Amino-4-nitro	M	175	100	4	3-Amino-5-nitro-2-hydroxybenzoic acid	20	(61)
2-Methoxy-4-formyl	M	175	100	4	3-Methoxy-5-formyl-2-hydroxybenzoic acid	57	(6)
2,3,5-Trimethyl	Na	—	—	—	3,4,6-Trimethyl-2-hydroxybenzoic acid	—	(254)
2,4,5-Trimethyl	Na	180	—	—	3,5,6-Trimethyl-2-hydroxybenzoic acid	33	(148)

* Naphthia or dioxane used as solvent.

† Xylene used as solvent.

TABLE 8
Mononuclear polyhydric phenols

Compound	Conditions				Products	Yield, per cent	References
	Metal or Marasse	Temperature	CO ₂ pressure	Time of heating			
		°C.	atm.	hours			
1,2-Dihydroxybenzene	Na (di)	145	56	43	2,3-Dihydroxybenzoic acid	58	(39, 209)
	M	225	100	4	2,3-Dihydroxybenzoic acid	72	(6, 32, 161, 183, 254)
1-Methyl-2,3-dihydroxybenzene	M	225	100	8	2,3-Dihydroxyterephthalic acid	81	
	M	175	50	5	4-Methyl-2,3-dihydroxybenzoic acid	—	(254)
1-Methyl-3,4-dihydroxybenzene	M	250	50	15	4-Methyl-2,3-dihydroxyisophthalic acid	14	
					5-Methyl-2,3-dihydroxybenzoic acid	—	(254)
1,3-Dihydroxybenzene*	M	300	100	1	5-Methyl-2,3-dihydroxyterephthalic acid	50	
	KHCO ₂	130	27	3.5	1,6-Dihydroxyisophthalic acid	74	(6, 36, 254)
1-Methyl-2,4-dihydroxybenzene*	KHCO ₂ or NaHCO ₂	—	—	0.25	2,4-Dihydroxybenzoic acid	51	(91, 19, 172, 222, 225, 227)
					2,6-Dihydroxybenzoic acid	47	
1-Methyl-3,5-dihydroxybenzene	M	210	50	14	3-Methyl-2,6(or 4,6)-dihydroxybenzoic acid	—	(144)
1-Methyl-2,6-dihydroxybenzene	N ₂	180	—	5	4-Methyl-2,6-dihydroxybenzoic acid	90	(254, 182, 216, 223)
1,3-Dimethyl-4,6-dihydroxybenzene*	NaHCO ₂	130	—	—	3-Methyl-2,4-dihydroxybenzoic acid	—	(104)
1-Amino-3,5-dihydroxybenzene*	KHCO ₂	80	—	6	3,5-Dimethyl-2,6-dihydroxybenzoic acid	—	(145)
1,4-Dihydroxybenzene	M	160	40	5	4-Amino-2,6-dihydroxybenzoic acid	—	(211)
					2,5-Dihydroxybenzoic acid	52	(254, 6, 32, 227)
1-Methyl-2,5-dihydroxybenzene	KHCO ₂	180	1	—	2,5-Dihydroxyterephthalic acid	34	
					4-Methyl-2,5-dihydroxybenzoic acid	—	(200, 31)
1,2,3-Trihydroxybenzene*	KHCO ₂	130	—	—	2,3,4-Trihydroxybenzoic acid	70	(144, 6, 224, 240, 247, 259)
	M	200	40	5	2,3,4-Trihydroxyisophthalic acid	95	(254)
3,4,5-Trihydroxybenzoic acid	KHCO ₂	180	1	12	2,3,4-Trihydroxyisophthalic acid	—	(32)
1,2,4-Trihydroxybenzene*	NaHCO ₂	100	—	1.5	2,4,6-Trihydroxybenzoic acid	33	(240, 254)
1,3,5-Trihydroxybenzene*	KHCO ₂	100	—	10 min.	2,4,6-Trihydroxybenzoic acid	55	(116, 32, 174, 233, 254, 258, 259)
1-Methyl-2,4,6-trihydroxybenzene	KHCO ₂	70	—	—	3-Methyl-2,4,6-trihydroxybenzoic acid	—	(213)
1,3-Dimethyl-2,4,6-trihydroxybenzene*	KHCO ₂	100	—	—	3,5-Dimethyl-2,4,6-trihydroxybenzoic acid	—	(20)

* Water used as solvent.

† Glycerol used as solvent.

TABLE 9
Dinuclear phenols

Phenol	Conditions				Products	Yield	References
	Metal or Marasse	Temperature	CO ₂ pressure	Time of heating			
		°C.	atm.	hours		per cent	
1-Naphthol	Na	135	36	1	1-Hydroxy-2-naphthoic acid	92	(4, 33, 62, 63, 106, 174, 194, 203, 207)
	M	160	50	—	1-Hydroxy-2-naphthoic acid	82	(254, 54, 185)
2-Naphthol	Na	130	—	—	2-Hydroxy-1-naphthoic acid	90	(207, 33, 106, 147, 174, 195, 196, 203, 243)
	M	160	50	—	2-Hydroxy-1-naphthoic acid	63	(254, 185)
	Na	235	—	10	2-Hydroxy-3-naphthoic acid	79	(115, 11, 34, 70, 108, 113, 147, 171, 215, 218, 219, 229, 230, 231)
	K	230	—	8	2-Hydroxy-3-naphthoic acid	—	(3)
					2-Hydroxy-6-naphthoic acid	60	
3-Methyl-1-naphthol*	Na	100	—	6	3-Methyl-1-hydroxy-2-naphthoic acid	—	(161)
5-Methyl-2-naphthol	Na	160	25	5	5-Methyl-2-hydroxy-1-naphthoic acid	—	(61, 156)
	Na	240	25	5	5-Methyl-2-hydroxy-3-naphthoic acid	—	(61)
6-Methyl-2-naphthol	Na/K	250	50	—	6-Methyl-2-hydroxy-3-naphthoic acid	—	(156)
7-Methyl-2-naphthol	Na	250	50	—	7-Methyl-2-hydroxy-3-naphthoic acid	—	(156)
8-Methyl-2-naphthol	Na	250	50	—	8-Methyl-2-hydroxy-3-naphthoic acid	—	(156)
6-Ethyl-2-naphthol	Na	250	50	—	6-Ethyl-2-hydroxy-3-naphthoic acid	—	(156)
6- <i>n</i> -Propyl-2-naphthol	Na	250	50	—	6- <i>n</i> -Propyl-2-hydroxy-3-naphthoic acid	—	(156)
5-Methoxy-1-naphthol	M (KHCO ₂)	220	—	3	5-Methoxy-1-hydroxy-2-naphthoic acid	90	(114)
5-Methoxy-2-naphthol	Na	260	50	10	5-Methoxy-2-hydroxy-3-naphthoic acid	—	(28)
6-Methoxy-2-naphthol	Na	260	50	10	6-Methoxy-2-hydroxy-3-naphthoic acid	—	(27)
7-Methoxy-2-naphthol	Na	260	50	10	7-Methoxy-2-hydroxy-3-naphthoic acid	—	(27)
6-Methylmercapto-2-naphthol	Na	280	60	10	6-Methylmercapto-2-hydroxy-3-naphthoic acid	—	(27)
5-Amino-1-naphthol	K	150	4	—	5-Amino-1-hydroxy-2-naphthoic acid	—	(261)
4-Amino-2-naphthol*	Na	110	—	—	4-Amino-2-hydroxy-1-naphthoic acid	—	(53)
	K	150	9	—	4-Amino-2-hydroxy-1-naphthoic acid	—	(53)
6-Carboxy-2-naphthol	K	250	120	10	2-Hydroxynaphthalene-3,6-dicarboxylic acid	—	(263)
5,6,7,8-Tetrahydro-1-naphthol	M	160	10	6	5,6,7,8-Tetrahydro-1-hydroxy-2-naphthoic acid	—	(214)
5,6,7,8-Tetrahydro-2-naphthol	K	170	—	6	5,6,7,8-Tetrahydro-2-hydroxy-3-naphthoic acid	70	(214)
	M	160	10	6	5,6,7,8-Tetrahydro-2-hydroxy-3-naphthoic acid	80	(214)
1,2-Dihydroxynaphthalene	Na (di) or K (di)	150	—	20	3,4-Dihydroxy-2-naphthoic acid	—	(193)
1,4-Dihydroxynaphthalene	Na (di)	170	—	30	1,4-Dihydroxy-2-naphthoic acid	90	(192, 100)
1,5-Dihydroxynaphthalene	M (KHCO ₂)	230	—	8	1,5-Dihydroxynaphthalene- <i>α,α</i> -dicarboxylic acid	—	(95, 96)

TABLE 9—*Concluded*

Phenol	Conditions				Products	Yield	References
	Metal or Marasse	Temperature	CO ₂ pressure	Time of heating			
		°C.	atm.	hours		per cent	
1,6-Dihydroxynaphthalene	M (KOH plus K ₂ CO ₃)	180	—	5	1,6-Dihydroxy- <i>x</i> -naphthoic acid	—	(95)
1,7-Dihydroxynaphthalene	Na (di) or M (di)	140	—	—	1,7-Dihydroxy- <i>x</i> -naphthoic acid	—	(109)
1,8-Dihydroxynaphthalene	Na (di) or K (di)	140	—	—	1,8-Dihydroxy- <i>x</i> -naphthoic acid	—	(109)
2,7-Dihydroxynaphthalene	Na	—	—	—	3,6-Dihydroxy-2-naphthoic acid	—	(201)
2-Hydroxybiphenyl	M	180	63	5	2-Hydroxybiphenyl-3-carboxylic acid	84	(246, 6, 111)
2-Hydroxy-5-ethylbiphenyl	M	225	—	14	2-Hydroxy-5-ethylbiphenyl-3-carboxylic acid	55	(111)
2-Hydroxy-5- <i>n</i> -propylbiphenyl	M	225	—	14	2-Hydroxy-5- <i>n</i> -propylbiphenyl-3-carboxylic acid	49	(111)
2-Hydroxy-5- <i>n</i> -hexylbiphenyl	M	225	—	14	2-Hydroxy-5- <i>n</i> -hexylbiphenyl-3-carboxylic acid	9	(111)
4-Hydroxybiphenyl	M	250	30	5	4-Hydroxybiphenyl-3-carboxylic acid	90	(246, 6)
4-Hydroxy-3-allylbiphenyl	Na	140	20	—	4-Hydroxy-3-allylbiphenyl-5-carboxylic acid	—	(74)
4,4'-Dihydroxybiphenyl	Na (di)	200	—	9	4,4'-Dihydroxybiphenyl- <i>x,x</i> -dicarboxylic acid	—	(210)
2-Cyclohexylphenol	M	175	100	4	2-Hydroxy-3-cyclohexylbenzoic acid	69	(6)
4-Hydroxydiphenylmethane	M	175	100	4	4-Hydroxybiphenylmethane-3-carboxylic acid	55	(6)
2,2'-Dihydroxydiphenylmethane	M	132	90	18	2,2'-Dihydroxydiphenylmethane-3-carboxylic acid	18	(38)
					2,2'-Dihydroxydiphenylmethane-3,3'(?)-dicarboxylic acid	5	
4,4'-Dihydroxydiphenylmethane	M	170	105	6.5	4,4'-Dihydroxydiphenylmethane-3-carboxylic acid	—	(38)
					4,4'-Dihydroxydiphenylmethane-3,3'-dicarboxylic acid	32	
2,2'-Dihydroxy-5,5'-dimethyldiphenylmethane	M	155	112	24	2,2'-Dihydroxy-5,5'-dimethyldiphenylmethane-3-carboxylic acid	4	(38)
					2,2'-Dihydroxy-5,5'-dimethyldiphenylmethane-3,3'-dicarboxylic acid	37	
3-Hydroxydiphenyl ether	Na	220	—	—	3-Hydroxydiphenyl-ether-4-carboxylic acid	—	(191)
Diphenylurea	M	260	50	5	2-Aminobenzoic acid	20	(136)
					4-Aminobenzoic acid	16	
					3-Phenylquinazoline-2,4-dione	—	
4-Hydroxybenzophenone	M	200	100	8	4-Hydroxybenzophenone-3-carboxylic acid	39	(6)
4,4'-Dihydroxybenzophenone	M	250	100	8	4,4'-Dihydroxybenzophenone-3-carboxylic acid	54	(6)
2-Benzamidophenol	M	175	100	4	2-Hydroxy-3-benzamidobenzoic acid	7	(6)
3-Benzamidophenol	M	175	100	4	2-Hydroxy-4-benzamidobenzoic acid	58	(6)
4-Benzamidophenol	M	230	100	8	2-Hydroxy-5-benzamidobenzoic acid	80	(6)
3-Benzylaminophenol	Na	130	100	12	2-Hydroxy-4-benzylaminobenzoic acid	10	(58)
4-Benzylaminophenol	M	175	100	8	2-Hydroxy-5-benzylaminobenzoic acid	12	(6)
4-Phenylazophenol	M	175	100	4	2-Hydroxy-5-phenylazobenzoic acid	42	(6)
4-Hydroxyhydrindene	Na	—	—	—	4-Hydroxyhydrindene-5-carboxylic acid	—	(254)

* Toluene used as solvent.

TABLE 10
Polynuclear phenols

Compound	Conditions				Products	Yield	References
	Metal or Marasse	Tempera- ture	CO ₂ pressure	Time of heating			
3-Hydroxyfluorene	Na or M	200	3	12	3-Hydroxyfluorene-2-carboxylic acid	—	(170)
6-Methyl-3-hydroxyfluorene	Na or M	200	3	12	6-Methyl-3-hydroxyfluorene-2-carboxylic acid	—	(170)
?-Methoxy-3-hydroxyfluorene	Na or M	200	3	12	?-Methoxy-3-hydroxyfluorene-2-carboxylic acid	—	(170)
4,7-Benzo-3-hydroxyfluorene	Na or M	200	3	12	6,7-Benzo-3-hydroxyfluorene-2-carboxylic acid	—	(170)
2-Hydroxyphenanthrene	Na	250	15	6	2-Hydroxy-1-phenanthroic acid	53	(251, 167)
3-Hydroxyphenanthrene	Na	250	30	6	3-Hydroxy-2-phenanthroic acid	57	(251, 167)
1-Hydroxyanthracene	Na	220	—	—	1-Hydroxyanthracene-2-carboxylic acid	—	(150)
8-Hydroxyfluoranthene	M	220	60	8	8-Hydroxyfluoranthene-9-carboxylic acid	—	(13)
Estrone	M	230	40	14	Estronemonocarboxylic acid	31	(252)
Diethylstilbestrol	M	200	40	—	Diethylstilbestroidicarboxylic acid	27	(252)
Hexestrol	M	260	40	12	Hexestroidicarboxylic acid	63	(252)

TABLE 11
Heterocycles

Compound	Conditions				Products	Yield per cent	References
	Metal or Marasse	Tem- pera- ture	CO ₂ pres- sure	Time of heating			
		°C.	atm.	hours			
2-Hydroxypyridine	Na	200	20	1	2-Hydroxypyridine-5-carboxylic acid	—	(244)
	M	250	130	8	2-Hydroxypyridine-5-carboxylic acid	45	(6)
3-Hydroxypyridine	Na	220	45	9	3-Hydroxypyridine-2-carboxylic acid	22	(22)
	K	220	45	9	3-Hydroxypyridine-2-carboxylic acid	3	(22)
					5-Hydroxypyridine-2-carboxylic acid	24	
	M	215	45	9	5-Hydroxypyridine-2-carboxylic acid	87	(22)
4-Hydroxypyridine	Na	220	50	—	4-Hydroxypyridine-3-carboxylic acid	52	(21)
	K	230	50	—	4-Hydroxypyridine-3-carboxylic acid	34	(21)
					4-Hydroxypyridine-3,5-dicarboxylic acid	4	
2-Hydroxyquinoline	Na, K, M	—	—	—	No carbonation	—	(244, 80)
6-Hydroxyquinoline	Na	175	—	8	No carbonation	—	(206)
	K	170	—	7	6-Hydroxyquinoline-5-carboxylic acid	90	(206)
8-Hydroxyquinoline	Na	150	—	8	8-Hydroxyquinoline-2-carboxylic acid	95	(208)
	M	200	130	4	8-Hydroxyquinoline-2-carboxylic acid	21	(6)
Pyrrole	K	220	1	—	Pyrrole-2-carboxylic acid	50	(41, 47, 48)
					Pyrrole-3-carboxylic acid	—	
2-Methylpyrrole	K	200	1	2	2-Methylpyrrole-3-carboxylic acid	—	(42)
4-Methylpyrrole	K	200	1	2	4-Methylpyrrole-2(or 3)-carboxylic acid	—	(42)
6-Hydroxy-2,3-diphenylindole	M	220	60	8	6-Hydroxy-3,3-diphenylindole-5-carboxylic acid	—	(7)
8-Hydroxy-2,3-diethyl- α -naphthindole	M	220	60	8	8-Hydroxy-2,3-diethyl- α -naphthindole-7-carboxylic acid	—	(7)
8-Hydroxy-2-octyl-3-ethyl- α -naphthindole	M	220	60	8	8-Hydroxy-2-methyl-3-ethyl- α -naphthindole-7-carboxylic acid	—	(7)
7-Hydroxy-2-phenyl- α -naphthindole	M	220	60	8	7-Hydroxy-2-phenyl- α -naphthindole-8-carboxylic acid	—	(7)
8-Hydroxy-2-phenyl- α -naphthindole	M	220	60	8	8-Hydroxy-2-phenyl- α -naphthindole-7-carboxylic acid	—	(7)
Carbazole	K	270	1	2	Carbazole-2-carboxylic acid	10	(15, 37)
1-Hydroxycarbazole	Na	220	40	21	1-Hydroxycarbazole-2-carboxylic acid	—	(199)
2-Hydroxycarbazole*	K	150	4	—	2-Hydroxycarbazole-3-carboxylic acid	85	(261, 190)
2-Hydroxy-9-methylcarbazole	Na	220	15	6	2-Hydroxy-9-methylcarbazole-3-carboxylic acid	—	(168)
2-Hydroxy-7,8,9,10-tetrahydro- α -benzocarbazole	M	220	60	8	2-Hydroxy-7,8,9,10-tetrahydro- α -benzocarbazole-3-carboxylic acid	—	(71)
2-Hydroxy-9-ethylcarbazole	Na	220	15	6	2-Hydroxy-9-ethylcarbazole-3-carboxylic acid	—	(168)

* Dichlorobenzene used as solvent.

TABLE 11—*Concluded*

Compound	Conditions				Products	Yield	References
	Metal or Marasse	Temperature	CO ₂ pressure	Time of heating			
		°C.	atm.	Hours		per cent	
3'-Hydroxy-7,8-benzocarbazole*	K	200	17	9	3'-Hydroxy-7,8-benzocarbazole-2'-carboxylic acid	60	(261)
1,8-Dihydroxycarbazole	K HCO ₂	200	50	20	1,8-Dihydroxycarbazole-2,7-dicarboxylic acid	—	(199)
6-Hydroxy-2-phenylbenzothiazole	M	220	65	—	6-Hydroxy-2-phenylbenzothiazole-5-carboxylic acid	—	(212)
7-Hydroxy-2-methyl- α -naphthothiazole	M	220	65	—	7-Hydroxy-2-methyl- α -naphthothiazole-8-carboxylic acid	—	(212)
8-Hydroxy-2-methyl- α -naphthothiazole	M	220	65	—	8-Hydroxy-2-methyl- α -naphthothiazole-7-carboxylic acid	—	(212)
2-Hydroxydibenzofuran*	K	200	8	—	2-Hydroxydibenzofuran-3-carboxylic acid	75	(261 169)
3-Hydroxydibenzofuran	M	220	—	10	3-Hydroxydibenzofuran-2-carboxylic acid	—	(169)
2-Allyl-3-hydroxydibenzofuran†	Na	140	20	—	2-Allyl-3-hydroxydibenzofuran-4-carboxylic acid	—	(74)
3-Hydroxydiphenylene sulfide	M	220	—	10	3-Hydroxydiphenylene sulfide 2-carboxylic acid	—	(169)
3-Hydroxydiphenylene sulfoxide	M	220	—	10	3-Hydroxydiphenylene sulfoxide 2-carboxylic acid	—	(169)
3-Hydroxydiphenylene sulfone	M	220	—	10	3-Hydroxydiphenylene sulfone 2-carboxylic acid	—	(169)
5-Hydroxycoumarane	K	130	—	—	5-Hydroxycoumarane- <i>o</i> -carboxylic acid	—	(73)
6-Hydroxy-2-methylcoumarane	K	130	—	—	6-Hydroxy-2-methylcoumarane-5-carboxylic acid	—	(73)
6-Hydroxy-3-methylcoumarane	K	130	—	—	6-Hydroxy-3-methylcoumarane-5-carboxylic acid	—	(73)
6-Hydroxy-3-methylcoumarone	K	130	—	—	6-Hydroxy-3-methylcoumarone-5-carboxylic acid	—	(73)
4-Hydroxycatechol ethylene ether	M	120	50	—	4-Hydroxycatechol ethylene ether 3(or 5)-carboxylic acid	—	(72)

† Naphtha or dioxane used as solvent.

TABLE 12
Ketones

Ketone	Conditions				Products	Yield	References
	Metal or amide	Temperature	CO ₂ pressure	Time of heating			
		°C.	atm.	hours		per cent	
Methyl ethyl*	NaNH ₂	-80	1	1	Propionylacetic acid§	25	(153)
Methyl <i>n</i> -propyl*	NaNH ₂	-80	1	—	<i>n</i> -Butyrylacetic acid§	30	(153)
Methyl isobutyl*	NaNH ₂	-80	1	—	Isovalerylacetic acid§	61	(153)
Methyl <i>n</i> -hexyl*	NaNH ₂	-80	1	—	<i>n</i> -Heptanoylacetic acid§	48	(153)
Methyl <i>tert</i> -butyl*	NaNH ₂	-80	1	—	Trimethylacetylacetic acid§	41	(153)
Diisopropyl*	NaNH ₂	-80	1	—	Isobutyrylisbutyric acid§	60	(153)
Diisobutyl*	NaNH ₂	-80	1	—	Isovalerylisovaleric acid§	38	(153)
Acetophenone*	NaNH ₂	-80	1	—	Benzoylacetic acid§	50	(153)
Butyrophenone*	NaNH ₂	-80	1	—	Benzoyl- <i>n</i> -butyric acid§	61	(153)
Cyclohexanone‡	NaNH ₂	35	1	3	Cyclohexanone-2-carboxylic acid	—	(83, 146, 153)
1-Methylcyclohexan-2-one‡	NaNH ₂	40	1	3	1-Methylcyclohexan-2-one-3-carboxylic acid	10	(83)
1-Methylcyclohexan-3-one‡	NaNH ₂	45	1	3	1-Methylcyclohexan-3-one-4-carboxylic acid	—	(83)
1-Methylcyclohexan-4-one‡	NaNH ₂	45	1	3	1-Methylcyclohexan-4-one-3-carboxylic acid	40	(83)
<i>p</i> -Menthone‡	Na	25	1	—	<i>p</i> -Menthonedicarboxylic acid	12	(29)
<i>d</i> -Isomenthone‡	NaNH ₂	25	1	0.5	<i>d</i> -Isomenthonedicarboxylic acid	—	(83)
					<i>d</i> -Isomenthonedicarboxylic acid		
Camphor‡	Na	30	1	—	Camphorcarboxylic acid	50	(29)
Tropinone‡	Na	—	1	—	After reduction: egonine and ψ -tropine- <i>O</i> -carboxylic acid	—	(260)

* Liquid ammonia used as solvent.

‡ Ether used as solvent.

‡ Low-boiling ligroin used as solvent.

§ Isolated as methyl ester.

carbonation experiments are buried in papers dealing with other topics or in the patent literature. Under the heading "Conditions: Metal or Marasse," Li, Na, K indicate that the salts of these metals were subjected to the Kolbe-Schmitt reaction; M indicates that the Marasse modification was used with potassium carbonate. The use of other carbonates is indicated by the appropriate formulas.

VII. SUMMARY

A survey of the Kolbe-Schmitt reaction with various modifications for the carbonation of phenols, heterocyclic hydroxy compounds, and certain ketones has been presented. The Kolbe-Schmitt procedure remains the standard commercial method for the preparation of aromatic hydroxy acids. The Marasse modification is more convenient for laboratory use. The course of the reaction is influenced by temperature, pressure, alkali metal, and the presence or absence of water. The mechanism of the reaction has not been rigorously established, but introduction of the carboxyl group by electrophilic substitution agrees with the known facts. Tables showing compounds carbonated, the experimental conditions, and the yields of the acids are given.

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