[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

# ORGANOMETALLIC COMPOUNDS IN THE KOLBE AND REIMER-TIEMANN REACTIONS

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A number of mechanisms have been proposed for the Kolbe and Reimer-Tiemann reactions. Among them are preliminary loose molecular complexes or coördination compounds; chelate (1a) and other additions followed by scissions, rearrangements, and eliminations (1b, c); and direct substitution. As is often the case where no decisive information is at hand, many of the proposed interpretations have some plausibility. The object of the present report is to present additional evidence (1d) for the possible intermediate functioning of of organometallic compounds.

Recent studies (2a), particularly by Kohler and co-workers and Fuson and co-workers, have provided convincing evidence that some metallic enolates react as true organometallic compounds with a series of typical reagents in which is included carbon dioxide.

RCCH <sub>3</sub>	$\rightleftharpoons \mathrm{RC}=\mathrm{CH}_2$	[C <sub>2</sub> H <sub>6</sub> MgI] F	C=CH2	$\rightleftharpoons$ [RC-C]	$H_2MgI$ [CO <sub>2</sub> ]	RCCH <sub>2</sub> CO	OH
				1			
0	$\mathbf{OH}$		OMgI	0		0	

Inasmuch as there are no significant differences in chemical behavior between enols and phenols, it may be permissible to carry over analogies from metal salts of enols to metal salts of phenols.<sup>1</sup> On such a basis the following equilibria may be set up for the sodium salts of phenol together with their reactions with carbon dioxide. A double allylic or  $\alpha, \gamma$ -rearrangement of [A] would result in the transposition of sodium (or equivalent electronic shifts) to give the *para*homologs of [B] and [C]. As is well known, some *p*-hydroxybenzoic acid is formed in the Kolbe reaction when sodium phenoxide is used, and much *p*-hydroxybenzoic acid results when potassium phenoxide is used. It is highly unlikely that sodium phenyl carbonate [D] is an intermediate which rearranges to a sodium salt of salicylic acid (1c). Also it is quite probable that the equilibria of [A], [B], and [C] are markedly displaced toward [A]; and that like most organometallic compounds and salts they may function largely as ions.

We are now reporting that when lithium phenoxide is treated in an ether suspension at atmospheric pressures with solid carbon dioxide no salicylic acid is formed, and that the phenol is recovered on acidification. Under corresponding conditions after lithium phenoxide in ether is refluxed with n-butyllithium (or with n-butylsodium in petroleum ether) a small but significant yield of salicylic acid results, probably in accordance with the following reaction.

$$C_{6}H_{5}OLi + n - C_{4}H_{9}Li \rightarrow o - LiC_{6}H_{4}OLi \xrightarrow{[CO_{2}][HCl]} o - HOOCC_{6}H_{4}OH$$
 [11]

<sup>1</sup> A specific, pertinent illustration is the generalized observation by Oddo (2 b) that the halogenomagnesium derivatives of various phenols give the corresponding hydroxy acids with carbon dioxide at high temperatures (250-270°) or, in some cases, in solvents like benzene and toluene.

Reaction [II] is a typical metalation process which almost invariably involves an *ortho* hydrogen, and which takes place very readily and in satisfactory yields with a polyphenol like resorcinol (3) and a polymethoxy compound like phloroglucinol trimethyl ether.<sup>2</sup> It is possible that the Kolbe reaction may involve intermediately formed organosodium compounds in accordance with one or more of the reactions described in [I] and by a secondary metalation reaction



like that pictured in [II]. In the metalation process, a compound like [B] or [C] would metalate [A] in an *ortho*-position. The validity of these postulates is, of course, influenced by the experimental conditions, which are unlike those of the Kolbe reaction.

The metalation of  $\beta$ -naphthol, which proceeds to a greater extent than that of phenol, is of added interest because of its bearing on the concept of fixed bond

<sup>&</sup>lt;sup>2</sup> The yield of 2,4,6-trimethoxybenzoic acid by *n*-butyllithium-metalation of phloroglucinol trimethyl ether is 65%. Mr. R. N. Meals has also observed that phloroglucinol trimethyl ether can be metalated in one hour at  $0^{\circ}$ .

structures in naphthalene.<sup>3</sup> If the bonds in naphthalene are essentially fixed, and if metalation involves an active enolic structure, then metalation of  $\beta$ -naphthol followed by carbonation and hydrolysis should give 2-hydroxy-1-naphthoic acid. Actually the acid isolated was 2-hydroxy-3-naphthoic acid [Reaction (III)].



It is, of course, possible that an enol is involved incidental to a shift of the double bonds in  $\beta$ -naphthol to give some 2,3-unsaturation. However, it is highly unlikely that there is any appreciable temperature effect under the very moderate carbonation conditions that would induce any initially formed 2-hydroxy-1-naphthoic acid (or its salt) to rearrange to the more stable 2-hydroxy-3-naphthoic acid. Under the conditions of the Kolbe reaction with  $\beta$ -naphthol, the sodium salt when heated with carbon dioxide under pressure gives the less stable 1-carboxylic acid at 120–145°, but the more stable 3-carboxylic acid between 200–250°.

The course of the Kolbe reaction is profoundly influenced by experimental conditions like pressure and temperature, and by the nature of the metal. Two additional illustrations are pertinent. First, although sodium  $\beta$ -naphthoxide under carbon dioxide pressure and in the temperature range 200–250° gives largely 2-hydroxy-3-naphthoic acid, the corresponding potassium salt under carbon dioxide pressure and in the temperature range 170–230° gives not only 2-hydroxy-3-naphthoic acid but 2-hydroxy-6-naphthoic acid in considerable yield (5). Second, there is a reversibility in the direction of reaction depending on whether the salt is that of potassium or sodium. For example, potassium salicylate when heated at 200° gives the potassium salt of *p*-hydroxybenzoic acid; whereas the sodium salt of *p*-hydroxybenzoic acid when heated at 200° gives the sodium salt of salicylic acid.

It is suggested that a mechanism involving intermediate organometallic compounds may be one of the stages involved in the Reimer-Tiemann reaction. Armstrong and Richardson (6) have presented satisfactory evidence for the following transformations.



<sup>3</sup> A general consideration of this problem has been presented by Fieser in Gilman's "Organic Chemistry," p. 148, John Wiley and Sons, New York (1943); see also Bergmann and Berlin (4).

The intermediate postulated has validity on the basis of related studies by v. Auwers and co-workers on alkylated phenols (7). It may owe its formation not only to direct nuclear substitution, but also to reactions like the following.



The Experimental Part also describes the metalation of thiophenol, and the halogen-metal interconversion reactions with o- and p-bromophenol. BrC<sub>6</sub>H<sub>4</sub>OH + n-C<sub>4</sub>H<sub>9</sub>Li  $\rightarrow$ 

$$LiC_{6}H_{4}OLi \xrightarrow{[CO_{2}]} \xrightarrow{[HOH]} HOOCC_{6}H_{4}OH$$

In conformity with other results on halogen-metal interconversions, the ortho isomer reacts distinctly more rapidly than the *para* compound.

#### EXPERIMENTAL PART

Phenol and n-butyllithium. To a filtered, cooled solution of n-butyllithium prepared (8) from 109.6 g. (0.8 mole) of n-butyl bromide and 11 g. (1.6 g. atoms) of lithium in 800 cc. of ether was added dropwise, with stirring, 18.8 g. (0.2 mole) of freshly distilled phenol in 50 cc. of ether. The mixture was refluxed for 19 hours and then carbonated in the customary manner by pouring on crushed solid carbon dioxide. The products isolated were 0.194 g. or 0.70% of salicylic acid (mixed melting point) and 17.8 g. or 94.6% of phenol. The yield of salicylic acid based on phenol not recovered was 13.2%.

Phenol and n-butylsodium. n-Butylsodium prepared from 13 g. (0.041 mole) of dibutylmercury and 10 g. (0.435 g. atom) of sodium wire in 200 cc. of petroleum ether (b.p. 28-38°) was treated with 2.82 g. (0.03 mole) of phenol. The mixture was stirred and refluxed for 19 hours and then poured on solid carbon dioxide. The products isolated were 0.43 g. or a 0.43% yield of salicylic acid (mixed m.p.) and 2 g. of phenol.

Thiophenol and n-butyllithium. A reaction mixture composed of approximately 0.2 mole of n-butyllithium in 400 cc. of ether and 11 g. (0.1 mole) of thiophenol in 50 cc. of ether was refluxed and stirred for 19 hours, and then carbonated by solid carbon dioxide. In addition to a recovery of 74.5% of the thiophenol, there was obtained 0.45 g. of an acid melting at 280° or at 286° after recrystallization from ethanol<sup>4</sup>. The yield of di-o-carboxyphenyl disulfide, (o-HOOCC6H4S-)<sub>2</sub>, was 2.94% or 11.6% based on thiophenol which had reacted.

<sup>&</sup>lt;sup>4</sup> Gattermann (9) reported the melting point 289°.

Anal. Calc'd for  $C_{14}H_{10}O_4S_2$ : neutral equiv., 153. Found: neutral equiv., 154.

The dibasic acid when treated with diazomethane gave di-o-carbomethoxyphenyl disulfide<sup>5</sup> melting at 131-132°.

What probably happened in this metalation was the initial formation of o-carboxythiophenol, which subsequently was oxidized atmospherically to the corresponding disulfide.

 $\beta$ -Naphthol and n-butyllithium. To approximately 0.2 mole of n-butyllithium in 200 cc. of ether was added slowly 0.1 mole of  $\beta$ -naphthol in 200 cc. of dry benzene. The solution was refluxed for 24 hours and then poured on solid carbon dioxide. The yield of crude 2-hydroxy-3-naphthoic acid (m.p. 209-215°) was 1.3 g. or 7%. After one crystallization from alcohol and water and two crystallizations from acetic acid and water the acid melted at 222-224°. The reported (11) melting point is 222-224°. There was recovered 8.9 g. or 62% of  $\beta$ -naphthol.

The acetoxy derivative, prepared by heating the acid with acetyl chloride, melted at 182–184°. The reported (11) melting point of 2-acetoxy-3-naphthoic acid is 184–186°.

 $\beta$ -Naphthyl ethyl ether and n-butyllithium. This experiment was carried out to provide additional confirmation of the 2-hydroxy-3-naphthoic acid, earlier experiments having shown that all ethers so far examined undergo *ortho*-metalation as is the case with the corresponding phenols. The 2-ethoxy-3-naphthoic acid, obtained subsequent to metalation of  $\beta$ -naphthyl ethyl ether by *n*-butyllithium, melted at 122-124°. The reported melting point is 124° (12).

Anal. Calc'd for C<sub>12</sub>H<sub>14</sub>O<sub>2</sub>: neutral equiv., 216.

Found: neutral equiv., 210.

The 2-ethoxy-3-naphthoic acid was de-ethylated by hydrobromic acid in glacial acetic acid and the resulting 2-hydroxy-3-naphthoic acid (m.p.  $221-222.5^{\circ}$ ) was shown by the method of mixed melting points to be identical with the 2-hydroxy-3-naphthoic acid obtained by metalation of  $\beta$ -naphthol.

A mixed melting point determination with the acetoxy derivative prepared from the deethylation product of 2-ethoxy-3-naphthoic acid with the acetoxy compound prepared from the 2-hydroxy-3-naphthoic acid formed by metalation showed these compounds to be alike.

o-Bromophenol and n-butyllithium. To approximately 0.1 mole of n-butyllithium in 200 cc. of ether was added slowly 0.05 mole of o-bromophenol in 25 cc. of ether. The solution was stirred for one-half hour with no external heating, after it had refluxed gently during the addition of the o-bromophenol, and then poured on solid carbon dioxide. The yield of salicylic acid (mixed m.p.) was 4.3 g. or 62%, and the acid melted at 158–159° without crystallization. There was recovered 2.9 g. or 32% of o-bromophenol.

*p*-Bromophenol and *n*-butyllithium. A mixture of 0.05 mole of *p*-bromophenol in 50 cc. of ether and approximately 0.1 mole of *n*-butyllithium in 200 cc. of ether was refluxed for two hours and then carbonated by solid carbon dioxide. The yield of crude *p*-hydroxybenzoic acid melting at 212-214° was 2.4 g. or 35%. After one crystallization from water the product melted at 214-215°.

When the reaction mixture of p-bromophenol and n-butyllithium was refluxed for only one-half hour the yield of p-hydroxybenzoic acid was 8%; and refluxing for one and one-half hours gave a 41% yield.

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## SUMMARY

The Kolbe and Reimer-Tiemann reactions may involve intermediate organometallic compounds arising from metallic phenoxides functioning as true organo-

<sup>5</sup> List and Stein (10) reported the melting point 130.5°; and Gattermann (9) the melting point 134°.

metallic compounds, and by metalations resulting in the formation of true organometallic compounds.

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