[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

The Preparation of Ketones by the Carbonation of Organolithium Compounds

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Introduction

Carbonation is one of the best methods for the characterization of reactive organometallic compounds because the acid formed by this reaction is, in general, readily isolated, purified and identified. However, the carbonation of phenyl-lithium has been reported to give only traces of benzoic acid,[1] and it has been stated that low yields of acid are observed in the carbonation of many Grignard reagents. Actually, the yields of acids from RMgX compounds, when carbonation is effected under optimal conditions,[2a] are excellent and in many cases approach theoretical values based on available Grignard reagent.[3] A low yield of benzoic acid from phenyl-lithium has been confirmed, and we have found that the poor yield is due to an uncommonly high yield (upward of 70%) of benzophenone. The carbonation of other organolithium compounds indicates that the reaction may be of value as a means of synthesizing some ketones.

Fortunately, it is possible to obtain good yields of acids by carbonating organolithium compounds under special conditions. An essential factor is a high local concentration of carbon dioxide, and this can be realized by procedures already described for the carbonation of Grignard reagents: namely, the addition of organometallic compound to solid carbon dioxide[4] or spraying the organometallic compound into an atmosphere of carbon dioxide.[2a,c]

Mechanism of Carbonations.—It is generally agreed that the following are the chief reactions involved in the carbonation of an RMgX compound.

$$\text{(I)}\quad RMgX + CO_2 \longrightarrow RCOOMgX$$
$$\text{(II)}\quad RCO_2MgX + RMgX \longrightarrow RCOR$$
$$\text{(III)}\quad RCOR + RMgX \longrightarrow R_3COH$$

At elevated temperatures and with a low concentration of carbon dioxide, the yield of acid is depressed and relatively large quantities of ketone and tertiary alcohol can be obtained.[4a,2b] Obviously, steric influences can operate to give high yields of acid (or/and ketone) where tertiary alcohol is a preponderant product in the absence of steric hindrance.

With aryl-lithium compounds, when carbon dioxide is bubbled into or

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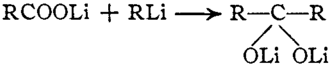
(1) Ziegler and Colonius, *Ann.*, **479**, 135 (1930).

(2) (a) Gilman and Parker, THIS JOURNAL, **46**, 2816 (1924); (b) Gilman and St. John, *Rec. trav. chim.*, **49**, 1172 (1930); (c) Gilman and Harris, *ibid.*, **50**, 1052 (1931); (d) Gilman and Zoellner, THIS JOURNAL, **53**, 1945 (1931).

(3) The hitherto exceptional cases, allyl- and β-styrylmagnesium bromides, have since been found to give satisfactory yields of acids.

(4) (a) Bodroux, *Bull. soc. chim.*, **31**, 24 (1904); (b) Spencer and Stokes, *J. Chem. Soc.*, **93**, 70 (1908).

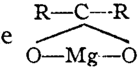
over the surface of the solution, the chief product is a ketone and practically no tertiary alcohol is formed. This indicates that the salt, RCOOLi, is converted to a di-lithium salt of a dihydroxymethane and not to the ketone.

(IV) 

$$\text{RCOOLi} + \text{RLi} \longrightarrow \text{R—}\underset{\text{OLi}\ \ \text{OLi}}{\text{C}}\text{—R}$$

(V) $\text{RCOR} + \text{RLi} \longrightarrow \text{R}_3\text{COH}$

Were the ketone formed as an intermediate, it is reasonable to suppose that it would react at once with the excess of RLi compound to give a tertiary alcohol. Benzophenone, for example, reacts (V) immediately and practically quantitatively with phenyl-lithium to give triphenylcarbinol.[1,5a]

A di-magnesium salt or its equivalent (like  $\underset{\text{O—Mg—O}}{\text{R—C—R}}$) may or may not be an intermediate in the carbonation of organomagnesium compounds, depending somewhat on the relative reactivity of the particular Grignard reagent. Organolithium compounds are distinctly more reactive than organomagnesium compounds[5b,6] and this would reflect itself in a tendency to add simultaneously or consecutively to the two carbonyl linkages in carbon dioxide to give the di-lithium salt. With RMgX compounds the —O metal linkage might be removed in accordance with Reaction (II) prior to addition of another molecule of RMgX to the available carbonyl group in the salt. Or the di-magnesium salt may lose magnesium oxide or its equivalent, more readily than the corresponding di-lithium salt loses lithium oxide, to give the ketone.

If Reaction (IV) is valid it might be expected that lithium benzoate would react with phenyl-lithium to give a satisfactory yield of benzophenone. This finds support in the formation of benzophenone in a 70% yield to the apparent exclusion of triphenylcarbinol. The reaction may find some application in the preparation of mixed ketones inasmuch as lithium *n*-butyrate and phenyl-lithium give a 62% yield of *n*-butyrophenone, $\text{C}_6\text{H}_5\text{COCH}_2\text{CH}_2\text{CH}_3$.

It is reasonable to conclude that if the reaction of a salt with an organolithium compound is arrested at the ketone stage because of the firmness of attachment of the metal to oxygen, then rubidium or cesium salts might be expected to give yields of ketone sufficiently high to commend the method as one of choice for the synthesis of mixed ketones, many of which are now relatively inaccessible.

[5] (a) Gilman, Zoellner and Selby, THIS JOURNAL, **54**, 1957 (1932); (b) Gilman and Kirby, *ibid.*, **55**, 1265 (1933).

[6] Incidentally, it was shown that phenyl-lithium is carbonated more rapidly, at about 0°, than phenylmagnesium bromide. These experiments were carried out quantitatively using a flowmeter and the color test for reactive organometallic compounds. The yield of benzoic acid from the phenylmagnesium bromide experiments was 85%.

Experimental Part

Carbonation of Organolithium Compounds.—Carbonation of phenyl-lithium under ordinary conditions used with Grignard reagents,[2a] gave 4% benzoic acid, 70% benzophenone and no triphenylcarbinol. In the spray-method,[2c] when phenyl-lithium in ether was added dropwise slowly, the yield of benzoic acid was 37% and the yield of triphenylcarbinol was 8.7%. However, when phenyl-lithium was added in jets of such size and so spaced that the temperature was maintained at 0°, the corresponding yields were 47.5 and 8.1%, respectively. The jet-wise addition of phenyl-lithium to solid carbon dioxide gave 60% of benzoic acid, 15.4% of benzophenone and no triphenylcarbinol. Under corresponding conditions, phenylmagnesium bromide gave a 90% yield of benzoic acid. The carbonation of phenyl-lithium at the boiling point of ether gave 1.6% of benzoic acid, 76% of benzophenone and no significant quantity of triphenylcarbinol.

Carbonation of *p*-tolyl-lithium, starting at 0° and ending at 15°, gave 1% of *p*-toluic acid and 77–81% of di-*p*-tolyl ketone. Under corresponding conditions, *o*-tolyllithium gave 35% of *o*-toluic acid. This relatively higher yield of acid is probably due to steric influences.

The yield of di-*n*-butyl ketone obtained by carbonating an ether solution of *n*-butyl-lithium cooled by an ice–salt bath was 45–50%. The ketone was characterized by its semicarbazone. Carbonation of 0.09 mole of *n*-butyl-lithium in benzene at room temperature gave 13% of the ketone and 0.9 g. of a liquid distilling at 102–105° (6 mm.). This probably is tri-*n*-butylcarbinol, and its formation reflects the greater reactivity of *n*-butyl- over phenyl-lithium.

Lithium Salts and Organolithium Compounds.—A suspension of 0.136 mole of lithium benzoate in ether was refluxed for five and one-half hours (to disappearance of color test) with 0.1 mole of phenyl-lithium. The yield of benzophenone was 70% and no triphenylcarbinol was isolated. With an ether–benzene medium, the time was ten hours and the yield of ketone 68%.

After refluxing lithium butyrate and phenyl-lithium in ether for eight hours, a 62% yield of *n*-butyrophenone was obtained. It was characterized by its semicarbazone.

In an orienting experiment, 0.1 mole of *n*-butyl-lithium, prepared from *n*-butyl chloride in benzene in a 55% yield, was refluxed with lithium *n*-butyrate (with benzene alone as the medium) for twenty-four hours to give a 10% yield of *n*-propyl *n*-butyl ketone. Apparently, ether is a better medium for such reactions.

Benzoyl Chloride and Phenyl-lithium.—Inasmuch as the reaction $C_6H_5COCl + C_6H_5MgI \longrightarrow (C_6H_5)_2C{=}O$ gives benzophenone in a 68.5% yield,[7] when the Grignard reagent is added to the acid chloride, it was of interest to learn whether a corresponding reaction with phenyl-lithium would give satisfactory yields of benzophenone. Actually, no benzophenone was obtained and the yield of triphenylcarbinol was 42%. The reverse mode of addition (benzoyl chloride to phenylmagnesium bromide) gives a 92% yield of triphenylcarbinol.[2b] It is probable that a study of optimal conditions like slow addition, marked cooling and high concentrations of benzoyl chloride will give ketones with organolithium compounds, but the method appears of little promise for the synthesis of ketones.

Miscellaneous.—The addition of 0.051 mole of benzoic acid to 0.102 mole of phenyllithium in ether gave 37.2% of benzophenone and 14.1% of triphenylcarbinol. The formation of triphenylcarbinol in this reaction is somewhat anomalous, because a reaction of lithium benzoate and phenyl-lithium gave 70% of ketone and no carbinol. One explanation for the formation of carbinol turns on the possible dehydration of benzoic acid

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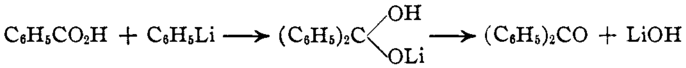
[7] Gilman and Mayhue, *Rec. trav. chim.*, **51**, 47 (1932).

by phenyl-lithium to give benzoic anhydride, which in turn should react with phenyl-lithium to give some "free" benzophenone, and this would react at once with phenyl-lithium to give triphenylcarbinol.

$$2C_6H_5COOH + 2C_6H_5Li \longrightarrow (C_6H_5CO)_2O$$
$$(C_6H_5CO)_2O + C_6H_5Li \longrightarrow C_6H_5CO_2Li + (C_6H_5)_2C{=}O$$
$$(C_6H_5)_2C{=}O + C_6H_5Li \longrightarrow (C_6H_5)_3COH$$

It has been suggested that the following competing reactions are equally reasonable to account for the formation of triphenylcarbinol.

$$C_6H_5CO_2H + C_6H_5Li \longrightarrow C_6H_5CO_2Li + C_6H_6$$



$$C_6H_5CO_2H + C_6H_5Li \longrightarrow (C_6H_5)_2C\begin{matrix}\diagup OH \\ \diagdown OLi\end{matrix} \longrightarrow (C_6H_5)_2CO + LiOH$$

In the latter (addition) reaction, the monolithium derivative would lose lithium hydroxide to form benzophenone which in turn would give triphenylcarbinol.

Finally, in order to determine whether organolithium compounds can be prepared without impairment of yield in the absence of an inert atmosphere,[5a] phenyl-lithium was prepared both under the usual conditions for the Grignard reagent and in an inert atmosphere. Each solution was treated with benzophenone and the yield of triphenylcarbinol from the phenyl-lithium prepared in an inert atmosphere was slightly higher than that obtained with no inert atmosphere. Accordingly, it is recommended that organolithium compounds be prepared in an atmosphere of nitrogen or hydrogen. Of course, closed containers are unnecessary.[5a]

Summary

Usual procedures for the carbonation of organolithium compounds give high yields of ketone and very little acid. The formation of acids for the characterization of organometallic compounds is markedly improved by the use of solid carbon dioxide or by the gas in the spray-procedure. A second method for the preparation of ketones, both simple and mixed, in satisfactory yields from organolithium compounds involves interaction with salts. A mechanism of carbonation is considered.

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