refluxed for 6 h with 8 ml each of concentrated HCl and ethanol. The mixture was diluted with water and extracted with ether. The aqueous layer was neutralized with sodium hydroxide and extracted with ether, and the ether evaporated. The oily residue was treated with acetic anhydride to yield 5.9 g (0.029 mol) of *p*-bromoacetanilide which, after crystallization from aqueous ethanol, melted at 165–167 °C. Thus at least 95% of the bromine in the starting imide remained intact during the reaction with *n*-butyllithium.

B. To 4.32 g (0.01 mol) of triphenylphosphine *N*-(4-bromophenyl)imide suspended in 50 ml of ether was added 10 ml of 1.8 M phenyllithium in benzene–ether. After 3 h one-half of the solution was treated with CO_2 in the usual manner, yielding 67% of 2-diphenylphosphinylbenzoic acid. The other half was treated with 0.005 mol of trimethylsilyl chloride, as described in A above, and yielded 1.25 g (50%) of diphenyl-2-trimethylsilylphosphine *N*-(4-bromophenyl)imide, identical with the product from A, thus establishing the position of the trimethylsilyl group.

Registry No.—**1a,** 2325-27-1; **2,** 2572-40-9; **6,** 57901-16-3; **10,** 57901-17-4; **11,** 57901-18-5; **12,** 57901-19-6; triphenylphosphine *N*-(*p*-bromophenyl)imide, 14987-96-3; diphenylmethylphosphine *N*-phenylimide, 57901-20-9; *n*-butyldiphenylphosphine *N*-phenylimide, 57901-21-0; phenyllithium, 591-51-5; diphenylmethylphosphine oxide, 2129-89-7; diphenylphosphinylacetic acid, 1831-63-6; *n*-butyldiphenylphosphine oxide, 4233-13-0; methyllithium, 917-54-4; *n*-butyllithium, 109-72-8; triphenyllead chloride, 1153-06-6; tetraphenyllead, 595-89-1; *p*-bromoacetanilide, 103-88-8.

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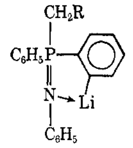
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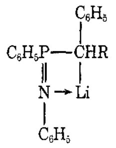
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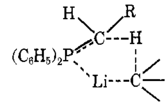
C

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Reactions of Carboxylic Acids with Organolithium Compounds

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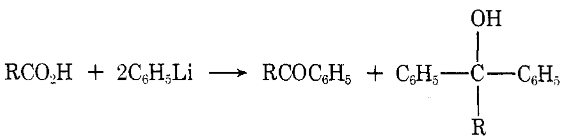
A series of carboxylic acids, RCO_2H, has been treated with a series of organolithium compounds, R′Li, to give, in most cases, a mixture of ketones, RCOR′, and carbinols, $R'_2C(OH)R$. A scheme is presented to account for the formation of these products and evidence in its support is given.

Recently we reported[1] that the interaction of equivalents of lithium carboxylates and organolithium compounds for a 24-h period gave mixtures of ketones and carbinols. It was anticipated that similar results would arise from the interactions of carboxylic acids (1 equiv) and organolithium compounds (2 equiv);[2] however, quite different results were obtained (vide infra).

In the present study a series of aliphatic acids (1 equiv) and one aromatic acid (1 equiv) were allowed to react with phenyllithium (2 equiv) for 0.5 h. In all cases mixtures of ketones and carbinols were obtained.


$$RCO_2H + 2C_6H_5Li \longrightarrow RCOC_6H_5 + C_6H_5-\overset{\displaystyle OH}{\underset{\displaystyle R}{C}}-C_6H_5$$

It was thought that refluxing the carboxylic acids with phenyllithium for periods greater than 0.5 h might lead to only ketonic products as was found[1] in the reactions of preformed lithium carboxylates with phenyllithium. However, refluxing *n*-butyric acid or benzoic acid (1 equiv) with phenyllithium (2 equiv) for varying periods of time gave essentially the same yields of ketone and tertiary alcohol (Table I).

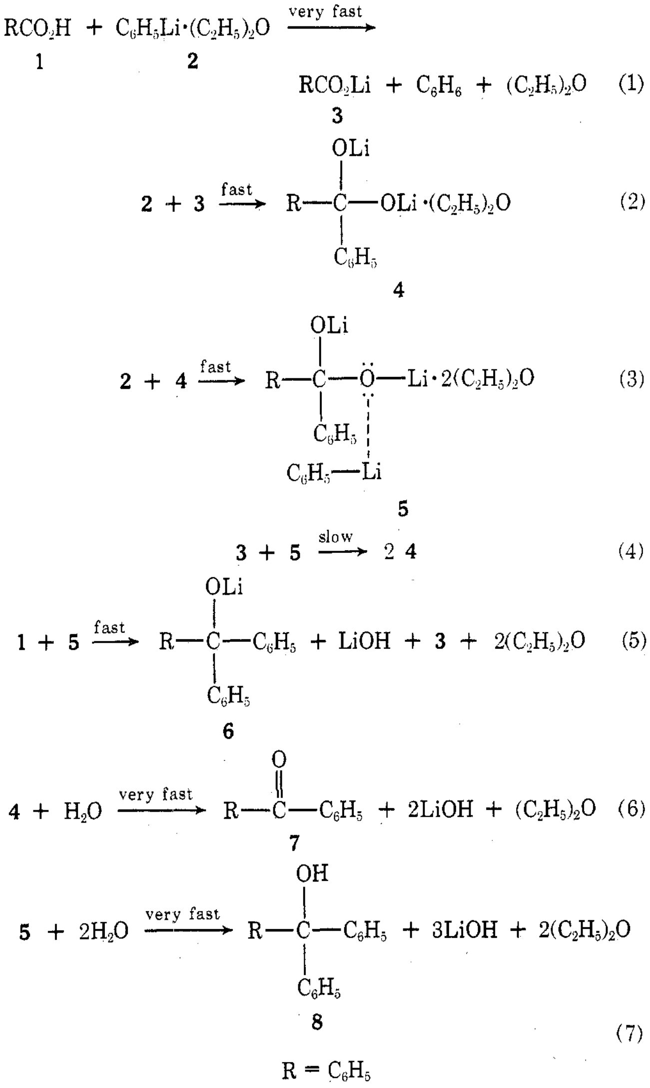
Table I. Reactions of *n*-Butyric and Benzoic Acids with Phenyllithium

RCO_2H, R	Reflux time, h	Products, % yield C_6H_5COR[a]	 $(C_6H_5)_2C(OH)R$[b]
n-C_3H_7	0.5	57	25
n-C_3H_7	24	60	29
C_6H_5	0.5	54	25
C_6H_5	24	66	25
C_6H_5	96	63	25

[a] Physical constants agree with literature values [C. R. Hauser, W. J. Humphlett, and M. J. Weiss, *J. Am. Chem. Soc.*, **70,** 426 (1948)]; in each case the carboxylic acid (1 equiv) was added to phenyllithium (1 equiv). [b] Physical constants agree with literature values [H. Masson, *C. R. Acad. Sci.*, **135,** 534 (1902)].

Several other aliphatic, aromatic, and heterocyclic acids were treated with phenyllithium to give mixtures of ketones and carbinols (Table II). In addition, the reactions of benzoic acid with six aliphatic organolithium compounds gave, in most cases, mixtures of ketones and carbinols (Table III).

The following scheme is proposed to explain the observed results, using the reaction of benzoic acid with phenyllithium as an example.



$$\underset{1}{RCO_2H} + \underset{2}{C_6H_5Li\cdot(C_2H_5)_2O} \xrightarrow{\text{very fast}} \underset{3}{RCO_2Li} + C_6H_6 + (C_2H_5)_2O \quad (1)$$

$$2 + 3 \xrightarrow{\text{fast}} \underset{4}{R\text{—}C(OLi)(C_6H_5)\text{—}OLi\cdot(C_2H_5)_2O} \quad (2)$$

$$2 + 4 \xrightarrow{\text{fast}} \underset{5}{R\text{—}C(OLi)(C_6H_5)\text{—}\ddot{O}\text{—}Li\cdot 2(C_2H_5)_2O \cdots C_6H_5\text{—}Li} \quad (3)$$

$$3 + 5 \xrightarrow{\text{slow}} 2\ 4 \quad (4)$$

$$1 + 5 \xrightarrow{\text{fast}} \underset{6}{R\text{—}C(OLi)(C_6H_5)\text{—}C_6H_5} + LiOH + 3 + 2(C_2H_5)_2O \quad (5)$$

$$4 + H_2O \xrightarrow{\text{very fast}} \underset{7}{R\text{—}C(=O)\text{—}C_6H_5} + 2LiOH + (C_2H_5)_2O \quad (6)$$

$$5 + 2H_2O \xrightarrow{\text{very fast}} \underset{8}{R\text{—}C(OH)(C_6H_5)\text{—}C_6H_5} + 3LiOH + 2(C_2H_5)_2O \quad (7)$$

$R = C_6H_5$

In this scheme, it is suggested (eq 1) that phenyllithium (2) reacts very rapidly, *but incompletely,* with benzoic acid (1) to give 3. Then (eq 2) 2 reacts with 3 by carbonyl addition to give 4. An adduct whose composition agrees with 4 has been isolated in the present study. It was further found that when 2 (2 equiv) is added all at once to 4 (1 equiv) in ether and the mixture is refluxed for 66 h, there is obtained almost equivalent amounts of ketone 7 (52%) and carbinol 8 (48%); this experiment indicates that 4 is unstable in the presence of 2. It might be argued that compound 4 loses lithium oxide to give the ketone, benzophenone, which then reacts to some extent with phenyllithium to give triphenylcarbinol. However, this argument appears to be untenable since the interaction of equivalents of lithium benzoate (3) and phenyllithium (2) for 24 h[1] gives only benzophenone (85%). Subsequently, 2 and 4 (eq 3) might react to give complex 5 which could participate in three reactions (eq 4, 5, and 7) to give the ketone and the carbinol or their precursors. Hydrolysis of 4 gives the ketone 7 (eq 6).

Table II. Reactions of Carboxylic Acids with Phenyllithium

Registry no.	RCO_2H,[a] R	Reflux time, h	Products, % yield[b] C_6H_5COR	$(C_6H_5)_2$-C(OH)R
64-19-7	CH_3	0.5	50	30
79-09-4	C_2H_5	0.5	60	28
107-92-6	n-C_3H_7	0.5	57	23
79-31-2	i-C_3H_7	0.5	58	28
75-98-9	$(CH_3)_3C$	0.5	65	26
142-62-1	n-C_5H_{11}	0.5	58	30
88-09-5	$(C_2H_5)_2CH$	0.5	49	22
65-85-0	C_6H_5	0.5	54	25
	C_6H_5	24	66	25
100-09-4	p-$CH_3OC_6H_4$	24	73	13
480-63-7	2,4,6-Trimethylphenyl	24	13	0
88-14-2	2-Furyl	2.5	47	5
527-72-0	2-Thienyl	2.5	32	10
98-98-6	2-Pyridyl	24	13	31

[a] In each case a 2:1 molar ratio of phenyllithium to carboxylic acid was used. [b] The physical constants of all the products agree with those reported in the literature.

Table III. Reactions of Benzoic Acid with Various Organolithium Compounds

Registry no.	RLi,[a] R	Products, % yield[b] C_6H_5COR	$R_2C(OH)C_6H_5$
917-54-4	CH_3	64	0
811-49-4	C_2H_5	43	0
2417-93-8	n-C_3H_7	54	28
109-72-8	n-C_4H_9	56	23
3525-31-3	n-C_5H_{11}	54	25
21369-64-2	n-C_6H_{13}	58	32
	C_6H_5	54	25

[a] In each case a 2:1 molar ratio of RLi to $C_6H_5CO_2H$ was used and the reflux time was 0.5 h. [b] The physical constants of all the products agree with those reported in the literature.

Equation 5 indicates that at some time during the reaction of phenyllithium (2 equiv) with benzoic acid (1 equiv), the acid 1 reacts with 5 in preference to reacting with 2. If this argument is valid, then treating 1 with a large quantity of 2 [so that there is always present much more phenyllithium (2) than 5] should prevent the reaction shown by eq 5 from taking place. If 3 is added at this point it should react with 5 (eq 4) to give essentially the ketone precursor, 4, and little or no tertiary alcohol should be formed. Thus, benzoic acid (1 equiv) was treated with phenyllithium (4 equiv) and the reaction mixture was refluxed for 0.5 h. Hydrolysis of an identical reaction mixture gave benzophenone (57.7%) and triphenylcarbinol (43%). Before hydrolysis, then, there should be present 58% of 4 and 43% of 5, the precursor of 6. Lithium benzoate (3, 2 equiv) was added at this point and the mixture was refluxed for an additional 24 h. Processing gave benzophenone (7, 81%), triphenylcarbinol (8, 8%), and recovered benzoic acid (1, 9%). Therefore, the results of this experiment suggest that when there is sufficient 2 present, the carboxylic acid 1 reacts preferentially with 2 rather than with 5. Subsequently, any 5 which is present is able to react with any available 3 to give 4, the precursor of the ketone.

When this last reaction was repeated except that the molar ratio of compounds 1:3:2 was 1:1:2 there was obtained benzophenone (7, 63%) and triphenylcarbinol (8, 24%). These results suggest that unless there is present a sufficiently large excess of 2 to convert most of 1 to 3, the acid 1 will react to an appreciable extent with 5 (eq 5), resulting in the formation of appreciable amounts of 6.

Experimental Section

General Procedure for the Reactions Involving the Addition of Carboxylic Acids to Organolithium Compounds in Re-

fluxing Ether. A solution of carboxylic acid in 75 ml of anhydrous ether is added to the ether solution of the organolithium compound at such a rate that the ether refluxes gently throughout the addition (usually requires about 2 h). The reaction mixture is subsequently refluxed for 0.5 h, unless indicated otherwise, and then is quenched by pouring onto crushed ice and water. The phases are separated and the aqueous phase is extracted with several portions of ether. The combined basic, ether phases are dried over Drierite, the solvent and low boilers are removed at atmospheric pressure, and the residue is fractionated under vacuum. The aqueous phase is acidified with concentrated hydrochloric acid and extracted with several portions of ether. The combined acidic, ether phases are processed in the same manner as the basic ether phases.

Reaction of Diethylacetic Acid (1 Equiv) with Phenyllithium (2 Equiv). From 1.2 mol (8.3 g) of lithium, 0.6 mol (94.2 g) of bromobenzene, and 0.3 mol (34.9 g) of diethylacetic acid, there was obtained 25.7 g (48.7%) of α,α-diethylacetophenone, bp 83–85 °C (1.4 mm),[3] oxime mp 89.4–90.0 °C,[3] which showed no depression when mixed with an authentic sample, and 11.1 g (21.8%) of 1,1-diphenyl-2-ethyl-1-butanol, bp 146–148 °C (1.4 mm).[4] The carbinol was dehydrated to the olefin 1,1-diphenyl-2-ethyl-1-butene, by refluxing 11 g of the carbinol with 15 ml of acetic anhydride and 20 ml of glacial acetic acid for 2 h.[5] The olefin was then oxidized by treatment with chromic acid in glacial acetic acid[5] to a mixture of diethyl ketone (2,4-dinitrophenylhydrazone, mp 155.6–156.2 °C,[6] alone and when mixed with an authentic sample) and benzophenone (2,4-dinitrophenylhydrazone, mp 241.5–242.0 °C,[7] alone and when mixed with an authentic sample).

Reaction of Benzoic Acid (1 Equiv) with *n*-Butyllithium (2 Equiv). From 0.36 mol of *n*-butyllithium and 0.18 mol (22.0 g) of benzoic acid, there was obtained 16.5 g (56.4%) of *n*-valerophenone and 6.0 g (22.8%) of di-*n*-butylphenylcarbinol. In addition, 5.5 g (25.0%) of benzoic acid was recovered.

The yields of *n*-valerophenone and di-*n*-butylphenylcarbinol were determined by the hydroxylamine hydrochloride titration method.[8] The lowest boiling fraction, *n*-valerophenone, bp 84–88 °C (1.2 mm),[9] gave a 2,4-dinitrophenylhydrazone, mp 164.0–164.6 °C,[10] alone and when mixed with an authentic sample.

The highest boiling fraction, di-*n*-butylphenylcarbinol, bp 111–112 °C (1.2 mm),[11] was dehydrated to the olefin 1-butyl-1-phenyl-1-pentene by refluxing the carbinol with acetic anhydride and glacial acetic acid for 2 h. The olefin was extracted with ether and subsequently oxidized with chromic acid in glacial acetic acid[5] to *n*-butyric acid (*n*-butyramide, mp 114.0–114.6 °C,[12] alone and when mixed with an authentic sample) and *n*-valerophenone (2,4-dinitrophenylhydrazone, mp 164.1–164.6 °C).[10]

Isolation of the Intermediate from the Reaction of Lithium Benzoate (1 Equiv) with Phenyllithium (1 Equiv) in Refluxing Ether. Lithium benzoate was added to phenyllithium and the reaction mixture was refluxed for 96 h. The ether was removed by filtration through a filter stick. The precipitate which remained was washed with three 200-ml portions of dry ether and the solvent was removed by use of the filter stick. The residual solid was dried at 20 mm pressure for 2 h at room temperature. From 0.3 mol (2.1 g) of lithium, 0.15 mol (23.6 g) of bromobenzene, and 0.15 mol (19.2 g) of lithium benzoate, there was obtained 41.2 g (96.3% yield) of a solid. The yield is based on the assumption that the solid is a monoetherated adduct of lithium benzoate and phenyllithium. Three samples of this solid were weighed and titrated with standard hydrochloric acid to give experimental equivalent weights of 143.0, 144.8, and 147.0. The calculated equivalent weight of a monoetherated adduct of lithium benzoate and phenyllithium is 142.9. A 5.0-g sample of this solid, upon hydrolysis, gave 2.8 g (90.0%) of benzophenone, mp 50.1–51.0 °C alone and when mixed with an authentic sample.

Reaction of Benzoic Acid (1 Equiv), Lithium Benzoate (2 Equiv), and Phenyllithium (4 Equiv). One equivalent of benzoic acid was added to 4 equiv of phenyllithium and the reaction mixture was refluxed for 0.5 h. Two equivalents of lithium benzoate was then added to the reaction mixture and the mixture was refluxed for 24 h. From 0.8 mol (5.6 g) of lithium, 0.4 mol (62.8 g) of bromobenzene, 0.1 mol (12.2 g) of benzoic acid, and 0.2 mol (25.6 g) of lithium benzoate, there was obtained 44.0 g (80.6%) of benzophenone, mp 50.1–51.0 °C, and 2.0 g (7.8%) of triphenylcarbinol, mp 159.5–159.9 °C.[13] In addition, 8.2 g (8.7%) of benzoic acid was recovered.

Reaction of Benzoic Acid (1 Equiv) with Phenyllithium (4 Equiv). From 0.8 mol (5.6 g) of lithium, 0.4 mol (62.8 g) of bromobenzene, and 0.1 mol (12.2 g) of benzoic acid, there was obtained 10.5 g (57.7%) of benzophenone, mp 50.1–51.0 °C, and 11.2 g (43.1%) of triphenylcarbinol, mp 159.6–160.0 °C.[13]

Registry No.—Lithium benzoate, 553-54-8; phenyllithium, 591-51-5.

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