

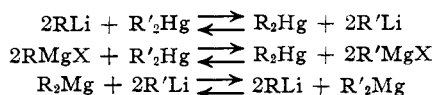
methoxybenzophenone. No unreacted *p*-methoxybenzoinitrile was found. This experiment was repeated, and a 50% yield of *p*-methoxybenzophenone was obtained.

In order to determine the extent of reaction of diphenylmagnesium with *p*-methoxybenzoinitrile under conditions comparable with the above reaction, the following experiment was carried out. A solution of 0.67 g. (0.005 mole) of *p*-methoxybenzoinitrile in a little ether was added to 50 cc. of 0.0085 molar diphenylmagnesium. After five minutes the mixture was hydrolyzed and worked up, as described above, to give 0.19 g. (18%) of *p*-methoxybenzophenone. From the ether layer was recovered 0.45 g. (67%) of unchanged *p*-methoxybenzoinitrile. From a

check experiment the yield of *p*-methoxybenzophenone was 19%.

Summary

It has been shown that some metal-metal interconversions involving the following organometallic combinations are reversible



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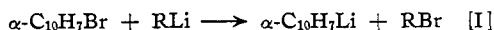
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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

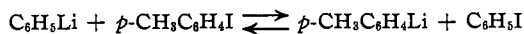
Reversible Halogen-Metal Interconversion Reactions¹

BY HENRY GILMAN AND R. G. JONES

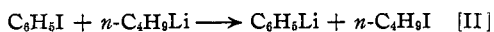
A study has been reported on some factors affecting the following typical halogen-metal interconversion reaction.²



It seemed of interest to examine the possible reversibility of halogen-metal interconversion reactions. For this purpose, the following combinations were selected: phenyllithium-*p*-tolyl iodide and phenyl iodide-*p*-tolyllithium. We are now reporting that this reaction is, in fact, reversible.



An X-M reaction, more typical from the viewpoint of synthesis, was next investigated: namely, that of an aryl halide with an alkyl lithium compound. No experimental evidence was obtained for the reversibility of the following reaction.



Under our experimental conditions, there was isolated a 71% yield of benzoic acid subsequent to carbonation,³ but no *n*-valeric acid. The absence of any evidence for the formation of *n*-butyllithium by a reversal of reaction [II] was not entirely unexpected, for in a related reaction [I] between α -bromonaphthalene and *n*-propyllithium, the yield of α -naphthoic acid (subsequent

to carbonation) was 97%.² We are of the opinion that despite the lack of present experimental support there is a reversible reaction between aryl halides and alkyl lithium compounds, but that the equilibrium with such combinations is displaced far to the right. It was surprising to observe that incidental to reaction [II] there was no significant coupling of the phenyllithium and *n*-butyl iodide to give *n*-butylbenzene. An earlier study² showed that α -naphthyllithium reacted rapidly with methyl iodide to give an 80% yield of α -methylnaphthalene.

Next, a third possible combination was examined: namely, an *alkyl* iodide and an *alkyl* lithium compound. The combinations selected were ethyl iodide-*n*-butyllithium and ethyllithium-*n*-butyl iodide. The reactions were carried out at a low temperature and were shown to be reversible: $\text{C}_2\text{H}_5\text{I} + n\text{-C}_4\text{H}_9\text{Li} \rightleftharpoons \text{C}_2\text{H}_5\text{Li} + n\text{-C}_4\text{H}_9\text{I}$.

Possible Applications.—Preceding papers in this series have shown that the X-M interconversion reaction with aryl halides and alkyl lithium compounds is a procedure of choice for the synthesis of some aryllithium compounds which are either difficultly accessible or which can be obtained by no other method. This applies particularly to aryl halides which contain functional groups, like azomethylene and carbonyl, that normally react very promptly with RLi compounds.

The demonstration of reversibility suggests that the reaction may be useful not only for comparing the relative reactivities of RM and RX

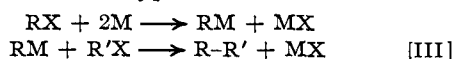
(1) Paper XXXVII in the series "Relative reactivities of organometallic compounds." The preceding paper is Gilman and Jones, *THIS JOURNAL*, **63**, 1439 (1941).

(2) Gilman and Moore, *ibid.*, **62**, 1843 (1940). The most recent reference on X-M interconversions is Langham, Brewster and Gilman, *ibid.*, **63**, 545 (1941).

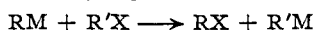
(3) In some earlier orienting experiments by Gilman, Langham and Moore, *ibid.*, **62**, 2327 (1940), there was obtained a 51% yield of benzoic acid.

compounds but also for throwing new light on the so-called relative negativities of radicals.

On the basis of present evidence,⁴ the Wurtz-Fittig reaction appears to involve either or both free radicals and organometallic compounds. If RM compounds are formed intermediately in the synthesis of R-R' types



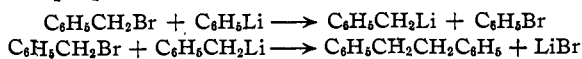
then an X-M interconversion reaction may take place in the coupling reaction [III].



Actually, an organosodium compound like *n*-butylsodium does show an interconversion reaction with α -bromonaphthalene to give, subsequent to carbonation, α -naphthoic acid.⁵

The literature of organometallic compounds contains many and varied reactions with halogen-containing compounds (apart from simple alkyl and aryl halides) in which the halogen is apparently replaced, at one stage or another, by a metallic combination. In a number of these cases it seems reasonable to postulate intermediate halogen-metal interconversions. Similar applications may possibly be extended to some reactions of RM compounds with compounds containing pseudo-halogens like CN and SCN.

The coupling reaction, examined by Späth and by Fuson,⁶ between benzyl halides and methylmagnesium iodide to give all possible coupling products, may or may not involve X-M interconversions: $\text{C}_6\text{H}_5\text{CH}_2\text{X} + \text{CH}_3\text{MgI} \rightarrow \text{C}_6\text{H}_5\text{CH}_2\text{CH}_3 + \text{CH}_3\text{CH}_3 + \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{C}_6\text{H}_5$. If interconversions take place in these systems then benzylmagnesium halides and methyl halides may participate to some extent in the coupling reactions. We are of the opinion that X-M interconversion plays no significant role in the $\text{C}_6\text{H}_5\text{CH}_2\text{X} + \text{CH}_3\text{MgI}$ reactions. In the first place, X-M reactions involving Grignard reagents generally take place slowly and at a lesser rate than coupling. Secondly, if the benzyl halide is benzyl chloride the RX compound formed by interconversion may be the volatile and lowly reactive methyl chloride. It is interesting that Wittig⁷ has proposed the reactions



(4) Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938, pp. 452-454.

(5) Studies by H. A. Pacevitz and F. W. Moore.

(6) See p. 425 of Ref. 4.

(7) Wittig, *Angew. Chem.*, **53**, 241 (1940).

Bromobenzene and dibenzyl were isolated, but no direct experimental evidence could be obtained for the intermediately formed, highly reactive benzyl lithium.

Experimental

Phenyllithium-*p*-Iodotoluene.—*p*-Iodotoluene, 5.45 g. (0.025 mole), in 25 cc. of ether was treated with 25 cc. of 1.10 molar phenyllithium solution. No heat effect or other observable change took place. After one minute the mixture was carbonated. The carbonation mixture, upon acidification, yielded *p*-toluic and benzoic acids which were separated by fractional crystallization from water and identified by the method of mixed melting points. The total yields of *p*-toluic and benzoic acids, calculated from the weight of the mixture and its neutralization equivalent, were 32% and 41%, respectively. In a duplicate experiment in which a fifteen minute reaction time was allowed, the yields of *p*-toluic and benzoic acids were 33.8% and 50.7%, respectively.

***p*-Tolylithium-Iodobenzene.**—A solution of 5.1 g. (0.025 mole) of iodobenzene in 25 cc. of ether was treated with 25 cc. of 1.01 molar *p*-tolylithium. The mixture was carbonated after one minute, and the acids were separated and identified as in the preceding experiment. The benzoic acid was further characterized by converting it to the anilide (mixed m. p.). The respective yields of *p*-toluic and benzoic acids were 45% and 30%.

p-Iodotoluene was obtained from the reaction and identified by converting it to di-*p*-tolylmercury using the catalyzed RLi reaction described in the following paper.⁸ After recrystallization from xylene and from acetone, the di-*p*-tolylmercury had a melting point and a mixed melting point with an authentic specimen of 235-237°.

When the above experiment was repeated allowing the *p*-tolylithium and iodobenzene to react for fifteen minutes before carbonating, the yields of *p*-toluic and benzoic acids were 30% and 47%, respectively.

Phenyllithium-*n*-Butyl Iodide.—A solution of 9.20 g. (0.050 mole) of *n*-butyl iodide in 25 cc. of ether at -15° was treated with 50 cc. of 1.1 molar phenyllithium. After one minute the solution was carbonated. The acidic material from the reaction was heated at 150° under 20 mm. pressure. No liquid distillate was obtained and not even an odor of valeric acid could be detected. The residue in the distilling flask was pure benzoic acid (73% yield).

The experiment was repeated using 0.050 mole of *n*-butyl iodide and 0.027 mole of phenyllithium and allowing a reaction time of thirty-five minutes at room temperature prior to carbonation. Again, no valeric acid could be found but a 71% yield of benzoic acid was obtained.

***n*-Butyllithium-Ethyl Iodide.**—In a 1-liter three-necked flask was placed 525 cc. of a 0.78 molar filtered ether solution of *n*-butyllithium (0.40 mole). This was cooled in a bath of acetone and carbon dioxide at -75° and rapidly stirred while a solution of 63 g. (0.40 mole) of ethyl iodide in 150 cc. of ether, cooled to -15°, was added during forty-five seconds. The mixture was maintained at -75° for thirty minutes and then carbonated by adding jetwise

(8) Gilman and Jones, *THIS JOURNAL*, **63**, 1443 (1941).

to a large excess of powdered, solid carbon dioxide in a 2-liter flask. The carbonation required fifteen minutes.

The reaction mixture was resolved by appropriate and standard procedures, and the following products were isolated and identified. (1) Ethyl iodide; characterized by conversion to ethylmercuric iodide⁹ by the Grignard reagent prepared from the ethyl iodide. (2) *n*-Butyl iodide (30% yield); characterized both by conversion to *n*-butylmercuric iodide and to *n*-valero- α -naphthylamide (via RMgI and α -naphthyl isocyanate¹⁰). (3) Propionic acid (43.4% yield); characterized by *p*-phenylphenacyl derivative.¹¹ (4) *n*-Valeric acid (34.8% yield);¹² characterized by *p*-phenylphenacyl derivative.

A similar reaction was carried out by adding 100 cc. of 0.87 molar *n*-butyllithium solution to 13.6 g. (0.087 mole) of ethyl iodide in 50 cc. of ether cooled to -70° . After fifteen minutes the mixture was carbonated. The respective yields of *n*-valeric and propionic acids were 38.4 and 42.2%. Identification of *n*-butyl iodide obtained from the reaction was made by converting it to *n*-butylmercuric iodide.

(9) Marvel, Gauerke and Hill, *THIS JOURNAL*, **47**, 3009 (1925).

(10) Gilman and Furry, *ibid.*, **50**, 1214 (1928).

(11) Drake and Bronitsky, *ibid.*, **52**, 3715 (1930).

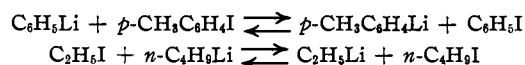
(12) The method for quantitatively estimating propionic and *n*-valeric acids in mixtures of the two was patterned after the procedure of Crowell, *ibid.*, **40**, 453 (1918).

Ethyllithium-*n*-Butyl Iodide.—A 100-cc. portion of 1.03 molar ethyllithium solution (0.10 mole) was placed in a 250-cc. three-necked flask and cooled to -70° in a bath of acetone and carbon dioxide. To this rapidly stirred solution was added 18.4 g. (0.10 mole) of *n*-butyl iodide in 50 cc. of ether. The mixture was stirred for fifteen minutes at -70° and then carbonated.

The following products were isolated and identified: (1) ethyl iodide; (2) *n*-butyl iodide; (3) propionic acid, 48.0% yield; (4) *n*-valeric acid, 36.4% yield. Each of these products was characterized by the derivatives mentioned in the preceding section.

Summary

The reversibility of the following halogen-metal interconversion reactions has been established



Some possible applications of the X-M interconversion reactions have been considered.

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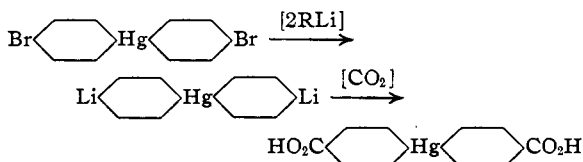
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The Catalytic Effect of Organolithium Compounds in Some Interconversion Reactions¹

BY HENRY GILMAN AND R. G. JONES

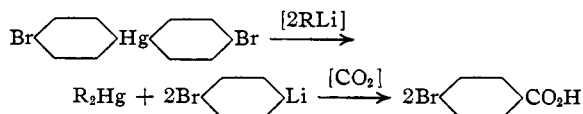
The two preceding papers on reversible metal-metal^{2a} and reversible halogen-metal^{2b} interconversions provide an explanation for an unusual reaction which is catalyzed by organolithium compounds. This reaction was discovered incidental to a broader study concerned with the introduction of water-solubilizing groups in organometallic compounds. It was hoped that the following typical sequence of reactions might occur.



Instead, a metal-metal interconversion took place and *p*-bromobenzoic and terephthalic acids, but no mercury containing carboxylic acids were formed.

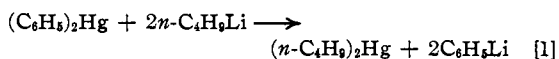
(1) Paper XXXVIII in the series: "Relative reactivities of organometallic compounds." The preceding paper is, Gilman and Jones, *THIS JOURNAL*, **63**, 1441 (1941).

(2) (a) Gilman and Jones, *ibid.*, **63**, 1439 (1941); (b) Gilman and Jones, *ibid.*, **63**, 1441 (1941).



The terephthalic acid owed its formation to a secondary halogen-metal interconversion reaction when excess RLi compound converted the *p*-bromophenyllithium to *p*-dilithiobenzene.

These abortive experiments suggested an examination of a more reactive halogen compound like *o*-bromoanisole which is known to undergo prompt Br-M interconversion.³ In a competitive reaction, a mixture of one equivalent of each of the following compounds—*o*-bromoanisole, diphenylmercury, and *n*-butyllithium—was allowed to react for varying intervals of time prior to carbonation. Reaction was apparently complete in one-half minute or less, and the sequence of transformations follows:



(3) Leading references to earlier work on halogen-metal interconversion reactions are contained in a paper by Gilman, Langham and Moore, *THIS JOURNAL*, **62**, 2327 (1940).