# THE ANALYSIS OF ORGANOLITHIUM COMPOUNDS*

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(Received May 5th, 1964)

There has been much interest in recent years in analytical methods for solutions of organometallic compounds. The necessity for reliable methods when structural and mechanistic studies are being carried out is obvious, and such studies are becoming increasingly common in the literature. Analytical procedures for organomagnesium compounds have been recently evaluated[1].

In the case of organolithium compounds there have been several studies aimed at developing a simple, accurate procedure[2-8,14-17]. It is well recognized that hydrolysis of an aliquot of an organolithium compound followed by titration with acid[2] leads to an analysis that is always high, because of the impossibility of excluding all traces of oxygen and moisture, which react with RLi to give other basic species. The most commonly used method of analysis for alkyllithium compounds has been a double titration in which benzyl chloride is used to destroy the RLi compound[4]. The method is more convenient to carry out than other procedures proposed, but several drawbacks have become apparent. Obviously low concentration values are obtained when the analysis is carried out on solutions of methyllithium and aryllithium compounds, and recent work has also indicated that the analysis is somewhat low for other alkyllithium compounds as well[6,9,14]. The implication is that benzyl chloride does not react quantitatively with RLi to give nonbasic products. The present investigation sought to overcome these difficulties by substituting other organic halides for benzyl chloride in the double titration procedure in order to improve the accuracy of the method while retaining its convenience and rapidity.

## EXPERIMENTAL

The organolithium reagents were prepared by conventional procedures in an atmosphere of dry, oxygen-free nitrogen. The solutions were filtered under nitrogen through a sintered glass funnel in order to remove insoluble material. The pipettes and flasks were baked in an oven at 110° and flushed with a stream of nitrogen until cool. The halides used in the titrations were dried over phosphorus pentoxide, decanted and then distilled. The ether employed was dried by storage over sodium wire.

### *Analytical procedure*

A 3 ml aliquot of the solution to be analyzed was withdrawn by pipette using a suction bulb and added to 10 ml of ether. The solution was hydrolyzed with 10 ml of distilled

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* Presented[13a] in part at the International Colloquium on Organometallic Compounds of the Centre National de la Recherche Scientifique, Paris, September 24–28, 1962.

water and titrated with standard acid, using phenolphthalein as indicator, to give the total alkali present. A second 3 ml aliquot was withdrawn and added to 10 ml of ether, containing 1 ml of the organic halide, under an atmosphere of nitrogen. The solution was swirled gently and allowed to stand for 2 min, after which it was hydrolyzed with distilled water and titrated immediately with standard acid, again using phenolphthalein as indicator.

In titrating the latter solution the end point is easily overstepped, since the aqueous layer decolorizes before the ether layer. Vigorous shaking near the end point is recommended. In some cases there is the possibility of interference from hydrolysis of the halide, so that the titration should be carried out without delay.

### *Reactions of lithium ethoxide and phenoxide with organic halides*

Solutions of lithium ethoxide and phenoxide were prepared by addition of an ether solution of the alcohol to finely cut lithium wire in ether under vigorous stirring. The resulting cloudy solutions were filtered under nitrogen through a sintered glass funnel. The solutions were titrated as in the above procedure, using standard sulfuric acid. After the acid titration, a Volhard titration was carried out in the case of the lithium ethoxide reactions in order to measure the halide ion released.

### *Reaction of triphenyltin chloride with phenyllithium*

The etheral solution of phenyllithium was added dropwise to a stirred solution of triphenyltin chloride in the minimum amount of tetrahydrofuran required for dissolution. An amount of triphenyltin chloride corresponding to a 25 % excess over the theoretical phenyllithium content of the ether solution was employed. At the completion of the addition, more dry ether was added, and stirring was continued for 4 h. The tetraphenyltin formed was filtered on a sintered glass funnel and washed twice with hot water and once with cold methanol. It was then dried in an oven and weighed. The product melted at 228–230° (mixed m.p.). The ether layer was evaporated, but no additional tetraphenyltin was obtained.

## RESULTS AND DISCUSSION

In the investigation a variety of organic halides was substituted for benzyl chloride in the standard double titration procedure for RLi compounds. Nineteen allyl halides, polyhaloalkanes and substituted benzyl halides were tested as possible reagents for titrations of alkyl- and aryllithium compounds. Many of the halides were those used in a previous study of the reactivity of octaphenylcyclotetrasilane with a large number of organic halogen compounds[10]. The halides are listed below in the order of increasing reactivity with phenyllithium, as judged from titration values obtained with them: *p*-methylbenzyl chloride, benzyl chloride, allyl chloride, *p*-bromobenzyl chloride, *sym*-tetrabromoethane, benzhydryl chloride, methyl iodide, *o*-chlorobenzyl chloride, benzyl bromide, *o*-methylbenzyl bromide, *sym*-tetrachloroethane, chloroform, *o*-bromobenzyl bromide, allyl bromide, allyl iodide, pentachloroethane, 1,2-dibromoethane, carbon tetrachloride, 1,1,2-tribromoethane, and $\alpha,\alpha,\alpha$-trichlorotoluene. The order given here is only approximate for some of the halides, which were used a few times and not investigated further. The halides giving the highest titration values were examined more thoroughly, with the exception of allyl iodide, which offers no advantages over other more readily available and more stable halides.

Attention was centered first on phenyllithium and methyllithium as compounds which give obviously low results with benzyl chloride. A number of halides gave higher results than benzyl chloride, and almost all the halides gave good precision when several titrations were made of a single preparation of RLi, as is shown in Table 1. In the titrations of phenyllithium, a gravimetric method of analysis was used as a check on accuracy. The reaction used was that with triphenyltin chloride, which produces tetraphenyltin, a compound virtually insoluble in ether. It is felt that the reaction is as nearly quantitative as could be obtained for a gravimetric analysis of RLi, as no side products can be isolated. Furthermore, the tetraphenyltin has a high melting point (230°), making drying of the sample quite convenient. In Table 2 the results of the triphenyltin chloride analysis are compared with double titration values using several organic halides. The halides giving the closest agreement with the yield of derivative are 1,2-dibromoethane* and carbon tetrachloride. 1,1,2-Tribromoethane gives slightly higher values, and α,α,α-trichlorotoluene is considerably higher.

TABLE 1

TITRATIONS OF METHYLLITHIUM

One preparation of methyllithium in diethyl ether was analyzed by the double titration procedure using several different organic halides. The molarity and an average value for the yield of the preparation are given.

| *RX compound* | *Molarity* | *Deviation, %* | *Yield, %* |
|---|---|---|---|
| None | 0.880 | | 84.5 |
| $PhCCl_3$ | 0.844, 0.845 | 0.1 | 81.1 |
| $BrCH_2CHBr_2$ | 0.820, 0.813 | 0.8 | 78.4 |
| $Br_2CHCHBr_2$ | 0.801, 0.800 | 0.1 | 76.8 |
| $BrCH_2CH_2Br$ | 0.793, 0.785 | 1.0 | 75.8 |
| $CH_2{=}CHCH_2Br$ | 0.759, 0.755 | 0.5 | 72.8 |
| $CHCl_3$ | 0.740, 0.744 | 0.5 | 71.3 |

TABLE 2

ANALYSIS OF PHENYLLITHIUM

Solutions of phenyllithium in diethyl ether were analyzed by double titration with several halides and by gravimetric determination of the tetraphenyltin formed on reaction with triphenyltin chloride.

| | *Molarity* | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | *None* | $PhCCl_3$ | $BrCH_2CHBr_2$ | $CCl_4$ | $BrCH_2CH_2Br$ | $C_2HCl_5$ | $CH_2{=}CHCH_2Br$ | $Ph_3SnCl$ |
| Run 1 | 0.980 | 0.945 | 0.926 | 0.909 | 0.907 | 0.872 | 0.835 | 0.905 |
| Run 2 | 1.07 | 1.02 | 0.972 | 0.966 | 0.962 | 0.924 | 0.870 | 0.961 |
| Run 3 | 0.942 | 0.861 | 0.801 | 0.800 | 0.785 | — | 0.686 | 0.797 |

The most probable reason for obtaining a titration value higher than the actual concentration is reaction of the organic halide with lithium alkoxide. Reactions of the

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* *Added in proof.* It has recently come to our attention that the use of 1,2-dibromoethane in double titrations of phenyllithium has been previously proposed[17], but the method was not investigated as to generality or compared with independent methods of analysis.

halides with lithium ethoxide and phenoxide were therefore carried out. The results are given in Tables 3 and 4. It is immediately clear that α,α,α-trichlorotoluene must be suspected of giving unreliable titration values due to considerable reaction with both ethoxide and phenoxide. With 1,1,2-tribromoethane there is an appreciable reaction with lithium ethoxide. Probably the 10% reaction observed in this case would not substantially alter the titration values for fresh preparations of RLi in which the concentration of alkoxide is low. However, 1,1,2-tribromoethane should certainly be used with caution where alkoxide concentration is suspected of being high. With 1,2-dibromoethane and carbon tetrachloride the interference should not be appreciable, as also with allyl bromide, which is discussed elsewhere[8b,11]. Thus, in the phenyllithium titrations in Table 2, the values with $PhCCl_3$ are undoubtedly too high. However, it is difficult to choose among 1,1,2-tribromoethane, carbon tetrachloride and 1,2-dibromoethane. Carbon tetrachloride has not been used regularly, because it is more difficult to obtain consistent results with that halide. Its reaction with RLi is extremely vigorous resulting in spattering the solution on the sides of the vessel, and the resulting solution is orange in color, making a phenolphthalein

TABLE 3

REACTIONS OF HALIDES WITH LITHIUM ETHOXIDE

Clear solutions of lithium ethoxide in diethyl ether were reacted with organic halides under the conditions used in the double titration. Acid titration with sulfuric acid was followed by Volhard titration to determine the amount of halide ion released.

| | *Halide* | *Normality* | *% Reaction* | |
|---|---|---|---|---|
| | | | *$H_2SO_4$* | *$AgNO_3$* |
| Run 1 | None | 0.140 | | |
| | $BrCH_2CH_2Br$ | 0.136 | 2.8 | 2.4 |
| | $BrCH_2CHBr_2$ | 0.125 | 10.7 | 7.9 |
| | $PhCCl_3$ | 0.106 | 24.2 | 31 |
| Run 2 | None | 0.429 | | |
| | $CCl_4$ | 0.426 | 0.7 | [a] |
| | $BrCH_2CH_2Br$ | 0.422 | 1.7 | [a] |

[a] There was no visible cloudiness on addition of aqueous $AgNO_3$.

TABLE 4

REACTIONS OF HALIDES WITH LITHIUM PHENOXIDE

A clear solution of lithium phenoxide in diethyl ether was treated with organic halides under the conditions used in the double titration. Titration was carried out using sulfuric acid.

| *Halide* | *Normality* | *% Reaction* |
|---|---|---|
| None | 0.144 | |
| $CCl_4$ | 0.144 | 0[a] |
| $BrCH_2CH_2Br$ | 0.142 | 1.4[a] |
| $BrCH_2CHBr_2$ | 0.143 | 0.7[a] |
| $PhCCl_3$ | 0.114 | 21 |

[a] There was no visible cloudiness on addition of aqueous $AgNO_3$.

end point more difficult to see. Also, carbon tetrachloride and chloroform both give low values when titrating methyllithium (see Table 1 for a comparison of chloroform with other halides). 1,1,2-Tribromoethane has been used regularly in this laboratory for the analysis of fresh preparations of phenyl- and methyllithium, because the $Ph_3SnCl$ treatment involves the isolation and purification of a derivative, and might be expected to give a slightly low analysis. However, 1,2-dibromoethane certainly gives a satisfactory analysis for normal work and is more readily available and in our experience is more stable when opened to the air at regular intervals than is 1,1,2-tribromoethane.

The titrations of methyllithium have not been similarly checked by an alternate method of analysis. However, the range of titration values obtained with various halides is quite similar to that with phenyllithium (compare Tables 1 and 2), and the authors feel that the statements above concerning the latter reagent apply also for methyllithium.

Titrations of *n*-butyllithium were investigated in some detail, particularly with allyl bromide, which had been previously proposed as a titrating agent for RLi[8] and for $R_3MLi$ (M = Si, Ge, Sn)[11]. It has been estimated[6,9] that the benzyl chloride double titration method gives an analysis which is about 5 % low for butyllithium in hydrocarbon solvents. The argument is based on the low solubility of lithium alkoxides in hydrocarbons, so that almost the total basic content of the solution should be due to RLi. Consequently, a new method of analysis was developed which consisted of oxidative titration with vanadium pentoxide[6]. Some caution is required with the titration because of the very strong oxidative power of vanadium pentoxide, which may also oxidize unsaturated carbon compounds present.

The conclusions about the accuracy of the benzyl chloride titration were questioned by another author[12]. However, with care taken in the preparation of an RLi compound in a hydrocarbon solvent, it should be possible to make RLi virtually the sole

TABLE 5

TITRATIONS OF *n*-BUTYLLITHIUM

Solutions of *n*-butyllithium were analyzed by double titration with 1,2-dibromoethane, allyl bromide and benzyl chloride. The results have been expressed as the percentage of the total basic content of the solutions which is due to C–Li.

| *Preparation* | *Percentage of total base due to C–Li* | | |
|---|---|---|---|
| | *$PhCH_2Cl$* | *$CH_2{=}CHCH_2Br$* | *$BrCH_2CH_2Br$* |
| BuLi in $Et_2O$[a], Run 1 | 88.1 | 93.6 | |
| BuLi in $Et_2O$[a], Run 2 | 90.1 | 95.1 | |
| BuLi in $Et_2O$[a], Run 3 | 76.3 | 81.2 | |
| BuLi in Hexane[b] | 94.7 | 98.6 | |
| BuLi in Hexane[c] | 97.1 | 99.2 | |
| BuLi in Hexane[c] | 97.0 | 99.2 | 99.1 |

[a] Prepared and analyzed under nitrogen atmosphere as described in the experimental section.
[b] Prepared under an argon atmosphere in a beverage bottle using lithium–vaseline dispersion, and introducing hexane and *n*-butyl chloride with a syringe through a Buna N liner. The analysis was carried out in a nitrogen-purged bottle with reagents being transferred by syringe. [c] A clear commercial preparation analyzed as above. The authors wish to express their appreciation to Dr. K. C. EBERLY of the Firestone Tire and Rubber Company for carrying out the preparation and analyses of the butyllithium in hexane.

contributor to the basic content of the solution. This criterion was taken as the best means for determining the accuracy of titrations of butyllithium. Table 5 shows typical titrations of the reagent with both benzyl chloride and allyl bromide, being expressed as the percentage of the total basic content of the solution which is due to RLi. The first three runs are for preparations in diethyl ether, and it may be noted that the allyl bromide values are consistently 5 % above those with benzyl chloride. This difference corresponds to the error previously estimated for the benzyl chloride method. The last two runs are for preparations in hexane solution, using rigorous conditions to exclude air and moisture (see footnote to the table). The high percentage found with the allyl bromide titrations is taken to indicate that the *n*-butyllithium in the solution is more completely consumed by allyl bromide than by benzyl chloride.

Recently, still another method of analysis for *n*-butyllithium in hydrocarbon solvents has been proposed[14]. The procedure, which involves thermometric titration with butanol, gives BuLi concentrations which are in essential agreement with those obtained by the $V_2O_5$ method and higher than is obtained by double titration with benzyl chloride[14]. The thermometric titration values quoted[14] for fresh preparations of BuLi in hydrocarbons show that approximately 99 % of the basic content of the solutions is due to RLi, in good agreement with the results quoted in Table 5 for double titrations with allyl bromide. It might be noted, however, that the double titration does not require the rather rigid and expensive experimental conditions necessary for the thermometric titration, and is much more convenient*.

In one instance in Table 5, 1,2-dibromoethane was also used for a titration in hydrocarbon solution, giving a result in excellent agreement with that from allyl bromide. Table 6 compares titrations of *n*-butyllithium in ether with allyl bromide and 1,2-dibromoethane. Values with the latter reagent are consistently slightly higher than those with allyl bromide, but the authors feel that the two reagents may be used interchangeably without significant sacrifice of accuracy.

TABLE 6

TITRATIONS OF *n*-BUTYLLITHIUM IN DIETHYL ETHER

Solutions of *n*-butyllithium in diethyl ether were titrated with both allyl bromide and 1,2-dibromoethane.

| | $CH_2{=}CHCH_2Br$ | $BrCH_2CH_2Br$ | % *Deviation* |
|---|---|---|---|
| Run 1 | 0.913 | 0.922 | 1.0 |
| Run 2 | 0.741 | 0.749 | 1.1 |
| Run 3 | 0.648 | 0.665 | 2.6 |

The use of 1,2-dibromoethane for the analysis of cyclopropyllithium has been reported recently**. In that case NMR spectroscopy was used in a rough check of the accuracy of the titration, with the conclusion that the analysis was satisfactory.

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* *Added in proof.* It was suggested to Mr. W. L. EVERSON that analyses be made using allyl bromide or 1,2-dibromoethane instead of benzyl chloride in the double titration method. A brief examination by him showed good agreement between the thermometric titration and double titrations using either of these two halides in place of benzyl chloride.

** The use of 1,2-dibromoethane was included in the presentation before the International Colloquium on Organometallic Compounds of the Centre National de la Recherche Scientifique, Paris, September 24–28, 1962. See ref. 13.

It should be noted that this investigation has not been extended to preparations of RLi compounds in tetrahydrofuran. The titrating agents described in this report, with the exception of allyl bromide, give unacceptably high results in titrations of silyl-, germyl- and tinlithium compounds in tetrahydrofuran[11]. The authors have expressed the opinion that there is finely divided or dissolved lithium metal in the above solutions causing the high titration values. Until the question is investigated further, the use of allyl bromide is suggested for titrations of RLi compounds in tetrahydrofuran.

In conclusion, of the halides so far examined, the normal research laboratory which desires occasional analyses of a variety of RLi compounds, will find it most convenient to use 1,2-dibromoethane for double titrations. This reagent gives reliable results for both alkyl- and aryllithium compounds in diethyl ether and for alkyllithium in hydrocarbons, and frequent redistillation is not required. The compound retains its efficacy for several months at least, when being used at frequent intervals. When $R_3MLi$ ($M = Si, Ge, Sn$) compounds are being analyzed, allyl bromide should be employed[11], and its use may be extended to the titration of alkyllithium compounds as well. Accuracy will be less satisfactory when allyl bromide is used with aryllithium compounds or methyllithium. These latter reagents may be titrated satisfactorily with 1,2-dibromoethane, but accuracy is probably slightly better with the more expensive 1,1,2-tribromoethane.

## ACKNOWLEDGEMENTS

This research was supported in part by the United States Air Force under Contract No. AF33(616)-6463 administered by Materials Laboratory, Wright Air Development Division, Wright-Patterson AFB, Dayton, Ohio. The authors are indebted to Dr. K. C. EBERLY for useful discussions and for the communication of his findings in this area of investigation.

## SUMMARY

A large number of organic halides was used in the double titration method of analysis for organolithium compounds. 1,2-Dibromoethane has been found to give a satisfactory analysis for alkyllithium compounds and phenyllithium. Titration employing the dibromoethane is recommended for general analytical use, although 1,1,2-tribromoethane probably gives a slightly more accurate analysis for fresh preparations of phenyl- and methyllithium. The use of allyl bromide in titrations of *n*-butyllithium in diethyl ether and hexane was also found to afford reliable results.

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