Mechanism of Halogen–Metal Interconversion between Aryl Bromides and Aryllithium Compounds. I. Equilibria

Hans J. S. Winkler and H. Winkler

Contribution from Monsanto Research SA, Zürich, Switzerland.

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Abstract: The halogen–metal interconversions between phenyllithium and aryl bromides are equilibrium processes. The equilibrium favors the formation of that organolithium compound which contains the more electronegative carbanion. The equilibrium constant for the exchange between phenyllithium and *p*-bromotoluene is insensitive to changes in temperature and is slightly lower in tetrahydrofuran than in diethyl ether.

Despite the accepted usefulness of halogen–metal interconversions for the preparation of organolithium compounds,[1] little is known about the mechanism of the reaction. We endeavored to study this reaction in detail to gain information about the modes of reaction of organolithium compounds. Through this knowledge it was expected that quantitative data could be collected on the reactivity of carbanions.

The system chosen for study was the halogen–metal interconversion between aryl bromides and aryllithium compounds. In this case the interconversion is conveniently slow for the measurement of rates.[2] Advantage was also recognized in studying a system in which the organolithium compound produced would be similar to the one initially present.

$$RBr + R'Li \rightleftharpoons RLi + R'Br$$

$$R, R' = \text{aryl groups}$$

Early work[3] had shown that the interconversion between iodobenzene and *p*-tolyllithium is reversible and more recently that in general the equilibrium proceeds toward the formation of the organolithium compound intuitively containing the more stable carbanion.[4]

The assumption has most widely been accepted that halogen–metal interconversions involve a four-center mechanism.

This view is perhaps founded in the observation that triptycyllithium may conveniently be prepared by halogen–metal interconversion of triptycyl bromide with butyllithium.[5] It was reasoned that since the backside of the bridgehead carbon is shielded one could not consider the interconversion as nucleophilic attack on carbon (which would not lead to exchange!). One then was led to the postulation of what amounted to simultaneous nucleophilic attack of carbanion on bromine and electrophilic attack of lithium cation on carbon.[5]

An indication that the interconversion may occur by nucleophilic attack on bromine is found in the halogen–metal interconversion between (−)-2-iodooctane and 2-butyllithium. The acid isolated on carboxylation indicated that the reaction proceeded by 20% over-all steric retention and 80% racemization.[6] It is particularly significant to note that in pure ether solvent the racemization was much more extensive than in ether–pentane mixtures. Similar effects of steric stabilities have been noted for carbanions in alkenyl- and cyclopropyllithium compounds.[7]

Results

For following the extent of reaction with time, the procedure first was adopted of hydrolyzing samples and analyzing for the aryl bromides and the hydrocarbons corresponding to the aryllithium reagents. This procedure soon was abandoned because the products of certain side reactions of the aryllithium compounds were likewise the hydrocarbons. It was thus not possible to follow the course of reaction proper by the concentrations of the organolithium reagents.

The kinetic procedure ultimately adopted depended on quenching the reacting system at the desired times by adding trimethylchlorosilane which undergoes an extremely fast and quantitative coupling reaction with the aryllithium compounds present. The samples of quenched reaction mixture then were analyzed by quantitative gas chromatographic techniques. Using the proper conditions the samples were analyzed for the following compounds: $ArSi(CH_3)_3$, $Ar'Si(CH_3)_3$, ArBr, Ar'Br, ArH, Ar'H, and biaryl compounds. By using an internal standard technique the change in the concentrations of these constituents with time could be calculated. The molar concentrations of $ArSi(CH_3)_3$ and $Ar'Si(CH_3)_3$ correspond to the concentrations of ArLi and Ar'Li.

Reaction proper:

$$ArLi + Ar'Br \rightleftharpoons ArBr + Ar'Li$$

Quenching reactions:

$$ArLi + (CH_3)_3SiCl \xrightarrow{\text{fast}} ArSi(CH_3)_3 + LiCl$$

$$Ar'Li + (CH_3)_3SiCl \xrightarrow{\text{fast}} Ar'Si(CH_3)_3 + LiCl$$

In the example the extent of halogen–metal interconversion thus could be estimated from the decrease in $[ArSi(CH_3)_3]$ and [Ar'Br] or from the increase in $[Ar'Si(CH_3)_3]$ and [ArBr] with time (formulas appearing in square brackets shall denote concentration terms).

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[1] R. G. Jones and H. Gilman, *Org. Reactions*, 6, 339 (1951).

[2] H. J. S. Winkler and H. Winkler, *J. Am. Chem. Soc.*, 88, 969 (1966).

[3] H. Gilman and R. G. Jones, *ibid.*, 63, 1441 (1941).

[4] D. E. Applequist and D. F. O'Brien, *ibid.*, 85, 743 (1963).

[5] G. Wittig and U. Schöllkopf, *Tetrahedron*, 3, 91 (1958).

[6] R. L. Letsinger, *J. Am. Chem. Soc.*, 72, 4842 (1950).

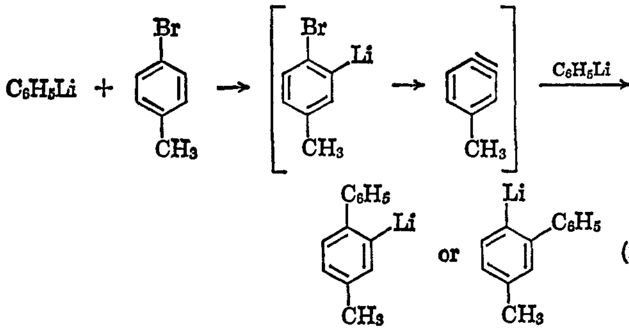
[7] D. J. Cram, "Fundametals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, pp 125, 130.

The technique used had the advantage of allowing ready detection of any irregularities such as the accidental introduction of moisture or side reactions. The presence of such effects would be detectable by irregularities of curves depicting the change in concentration of reactants and products with time. That such effects are not dominating was deduced from the symmetry of the plots, an example of which is presented in Figure 1.

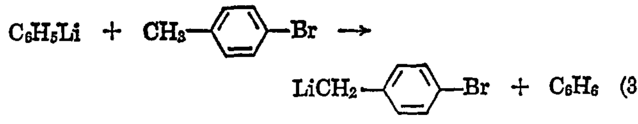
By approaching the equilibrium from either side on a preparative scale and isolating the *p*-tolyltrimethylsilane (starting from phenyllithium and *p*-bromotoluene) and *p*-bromotoluene (starting from *p*-tolyllithium and bromobenzene) it was established that lithium and bromine exchanged positions without causing isomerization.

Side Reactions. Since organolithium compounds in general are very reactive it became necessary to establish that possible side reactions proceeded at noncompeting rates under the conditions chosen. For the system Ar = C_6H_5, Ar′ = $CH_3C_6H_4$, the following side reactions were considered.

$$C_6H_5Li + C_2H_5OC_2H_5 \longrightarrow C_6H_6 + C_2H_4 + LiOC_2H_5 \quad (1)$$



(2)



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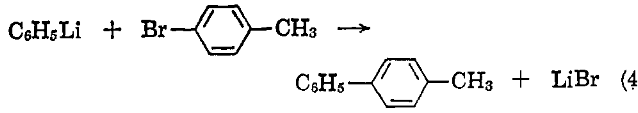

(4)

The reactions 1–3 involve metalations. Reaction 1 could have been detected by a faster decrease in [C_6H_5Li] than in [p-$CH_3C_6H_4Br$], and from an increase in [C_6H_6] corresponding to the difference in decrease of [C_6H_5Li] and [p-$CH_3C_6H_4Br$]. Such an effect although detectable after extended reaction times was not apparent within the period of the kinetic study.[2]

Reaction 2 also would cause nonequivalent decrease in [C_6H_5Li] and [p-$CH_3C_6H_4Br$], if phenyllithium adds appreciably to the tolyne formed. This effect might not be ascertained readily. Therefore the exchange was performed in the presence of diphenylisobenzofuran. If benzyne intermediates were formed at appreciable rates then the endoxide should have been formed in isolable amount, which it was not.

Reaction 3 should have been detectable by an increase in [C_6H_6] corresponding to a difference between the extent of decrease of [C_7H_7Br] and the increase of [C_6H_5Br]. Since such an effect was not observed this side reaction also was neglected. Reaction 4 leading to 4-methylbiaryl by nucleophilic substitution on aromatic carbon would have caused the same unsymmetrical effect as was discussed under reaction 3. That this was not true to an appreciable extent within the range depicted in Figure 1 is evident. However, this reaction may be responsible for the 5–10% yields of 4-methylbiphenyl present after 24 hr of reaction time.

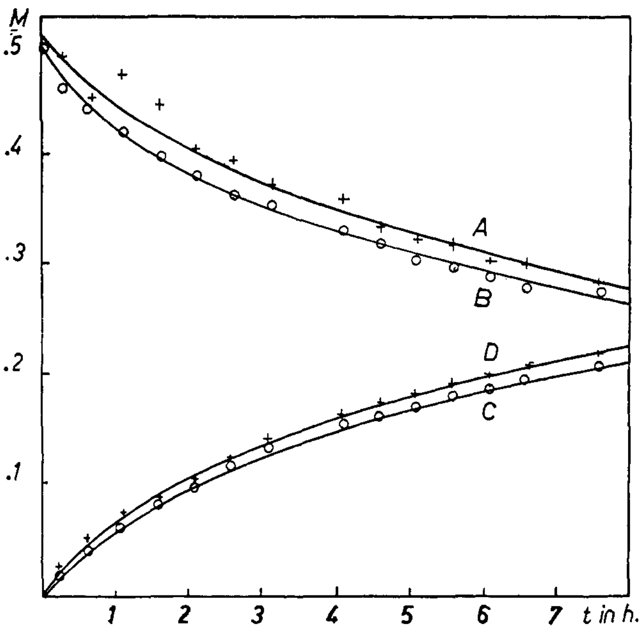

Figure 1. Halogen–metal interconversion between C_6H_5Li and p-$CH_3C_6H_4Br$.

$$\begin{tikzcd} C_6H_5Li + \underset{B}{p\text{-}CH_3C_6H_4Br} \arrow[r, shift left] \arrow[d, "(CH_3)_3SiCl"'] & \underset{C}{C_6H_5Br} + p\text{-}CH_3C_6H_4Li \arrow[l, shift left] \arrow[d, "(CH_3)_3SiCl"'] \\ \underset{A}{C_6H_5Si(CH_3)_3} & \underset{D}{p\text{-}CH_3\text{-}C_6H_4Si(CH_3)_3} \end{tikzcd}$$

Preparation of Aryllithium Reagents. For the purpose of this study the aryllithium reagents were prepared by one of two routes.

$$ArBr + 2Li \longrightarrow ArLi + LiBr \quad (A)$$

$$Ar_2Hg + 2Li \longrightarrow 2\,ArLi + Hg \quad (B)$$

The aryllithium reagent prepared by *route A* is called *salt containing* since it contains 1 mole of lithium bromide per mole of aryllithium reagent. Aryllithium reagents prepared by *route B* are called *salt free*.

Salt-free aryllithium reagents in general are more reactive than salt-containing reagents.[2,8] This is true as well for the side reactions as for the reaction proper. The extent of solvent metalation was demonstrated by maintaining ether solutions of salt-free phenyllithium and *p*-tolyllithium at 25° for 24 hr in sealed tubes and then deuterolizing. Analysis of the benzene and toluene fractions collected showed that metalation accounted for the consumption of *ca.* 30% of the aryllithium reagents. The extent of consumption within 6–8 hr was estimated not to influence seriously the rate data for halogen–metal interconversion.

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(8) G. Wittig and E. Benz, *Ber.*, **91**, 873 (1959), and R. Waack and M. A. Doran, *Chem. Ind.* (London), 496 (1964).

Halogen–Metal Interconversions as Equilibrium Processes. Evidence for the halogen–metal interconversions studied being true equilibrium processes is summarized in Table I. The exchange of lithium for bromine between a phenyl and a *p*-tolyl group was studied by performing the exchanges from either side of the equilibrium and by varying the initial concentrations.

$$C_6H_5Li + p\text{-}CH_3C_6H_4Br \rightleftharpoons C_6H_5Br + p\text{-}CH_3C_6H_4Li$$

The entries under the heading K_{obsd} are calculated by substituting the experimentally found equilibrium concentrations into the classical expression for the equilibrium constant for the reaction as written. The deviation from the mean corresponds to the type precision which can be expected from the techniques used. It is important to recognize that although systems involving salt-free phenyllithium reagents approach equilibrium faster than do systems with salt-containing reagents,[2] the position of the equilibrium is unaltered (systems 6 and 7 *vs.* 1–5).

Table I. Position of Equilibrium in the Halogen–Metal Interconversion

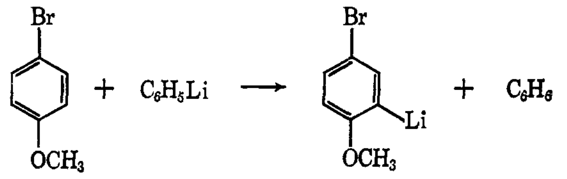
System no.	C_6H_5Li +	p-$CH_3C_6H_4Br$ ⇌	C_6H_5Br +	p-$CH_3C_6H_4Li$	
		Initial Concn[a]			
1	0.60	0.60	0	0	
2	0	0	0.50	0.50	
3	0.10	0.30	0	0	
4	0.45	0.30	0	0	
5	0.60	0.30	0	0	
6	0.29	0.28	0	0	
7	0.50	0.26	0	0	
		Equilibrium Concn			K_{obsd}[b]
1	0.328	0.334	0.254	0.259	0.60[b]
2	0.192	0.256	0.196	0.167	0.67[b]
3	0.014	0.233	0.052	0.032	0.52[b]
4	0.154	0.130	0.102	0.110	0.56[b]
5	0.372	0.119	0.139	0.161	0.50[b]
6	0.059	0.124	0.080	0.051	0.55[b]
7	0.281	0.107	0.132	0.139	0.61[b]

[a] The organolithium compounds used as starting materials were salt containing in systems 1–5, and salt free in systems 6 and 7. [b] K_{obsd} values = $[C_6H_5Br][p\text{-}CH_3C_6H_4Li]/[C_6H_5Li][p\text{-}CH_3C_6H_4Br]$ independent of side from which the equilibrium is approached.

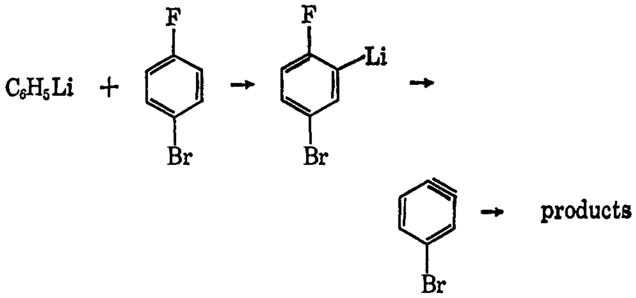
Equilibrium is attained after 10–20 hr. After such reaction times the consumption of both organolithium reagents and aryl bromides becomes evident by the appearance of several additional compounds of the biaryl type. This is the reason why the summation of molarities for the aryl groups separately is smaller than the starting concentration of that group.

Equilibrium Data for Various Halogen–Metal Interconversions. The halogen–metal interconversions between phenyllithium (salt containing) and several substituted aryl bromides (ZC_6H_4Br) were studied. The choices of substituents are limited because certain side reactions are favored by certain substituents.

Thus bromoanisole (Z = OCH_3) undergoes facile metalation in the position *ortho* to the methoxyl group.[9]



Fluorobromobenzenes (Z = F) are metalated in the position *ortho* to the fluoro substituent.[10] The metalated product undergoes lithium fluoride elimination causing benzyne formation.



A limited number of substituted bromobenzene derivatives were studied. The results of the equilibrium data are shown in Table II.

Table II. Equilibrium Constants for Interconversion between Phenyllithium and Aryl Bromides[a]

Substituent Z in BrC_6H_4Z	σ value of Z	K_{obsd}[b]
p-CH_3	-0.170	0.60 (0.67)
m-CH_3	-0.069	0.88 (0.84)
p-C_6H_5	$+0.009$	3.78 (3.79)
p-Cl	$+0.226$	53
m-CF_3	$+0.415$	289
p-F	$+0.062$	...[c]
p-OCH_3	-0.268	...[d]

[a] All reactions were performed in ether at 25.0° using salt-containing phenyllithium. The numbers in parenthesis represent averages of equilibrium constants obtained by approaching the equilibrium from the right. They could not be obtained for Z = *p*-Cl and Z = *m*-CF_3. [b] K_{obsd} = $[C_6H_5Br][ZC_6H_4Li]/[C_6H_5Li][ZC_6H_4Br]$. [c] Side reaction dominated, metalation *ortho* to F. [d] Side reaction dominated, metalation *ortho* to OCH_3.

Solvent and Temperature Effects. The marked influence of the medium on the rate of halogen–metal interconversion has already been demonstrated as has the independence of the equilibrium position on the medium.[4] Table III lists the results obtained for various temperatures in diethyl ether and tetrahydrofuran. The attainment of equilibrium was demonstrated by determining equilibrium concentrations over a time span exceeding that necessary for reaching equilibrium. For convenience, equilibration was approached (in ether) at room temperature and then at the given temperatures. This was not necessary in tetrahydrofuran since equilibration was faster by at least a factor of 10^2–10^3.

Discussion

It is evident from the results compiled in Table I that the halogen–metal interconversion between aryl-

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(9) G. Wittig, G. Pieper, and G. Fuhrmann, *Ber.*, 73, 1197 (1940).

(10) G. Wittig and L. Pohmer, *Angew. Chem.*, 67, 348 (1955); H. Gilman and R. P. Gorsich, *J. Am. Chem. Soc.*, 78, 2217 (1956).

Table III. Temperature Dependence of Equilibrium Constants[a] for Phenyllithium and *p*-Bromotoluene

In ether			In tetrahydrofuran		
Temp, °C	Time[b]	K_{obsd}[c]	Temp, °C	Time[d]	K_{obsd}[c]
25	18	0.36	25	0.16	0.39
	25	0.50		0.45	0.35
	48	0.60		2.0	0.42
	72	0.55		24.0	0.43
+10	24	0.55	+10	1.0	0.43
	72	0.60		2.3	0.45
	144	0.62			
0	28	0.38	0	1.0	0.37
	52	0.44		2.5	0.37
	120	0.49			
−10	24	0.54	−10	1.25	0.39
	72	0.60		2.5	0.42
	198	0.55			

[a] For interconversion between phenyllithium and *p*-bromotoluene, starting concentration of both *ca.* 0.3 *M*. [b] Time in hours, at a given temperature, after equilibration at 25°. [c] Same convention as in Table I. [d] Time in hours, after mixing at a given temperature.

lithium compounds and substituted bromobenzenes is an equilibrium process. It remains to clarify whether the magnitude of the equilibrium constant is a reasonable measure of the relative carbanion stabilities of the organolithium compounds involved.[11]

The classical expression for the equilibrium constant is valid for the exchange between monomeric organolithium compounds and aryl bromides. This is also the expression which would conveniently express the relative stabilities of organolithium reagents or the carbanions thereof.

It has been shown, however, that organolithium reagents are usually dimeric or polymeric aggregates and that the extent of association is dependent on the solvent.[12,13] The aggregate present in salt-containing phenyllithium is still more complex because of the additional association of the organolithium reagent with lithium bromide.[12,14] Whether such aggregates influence the over-all position of the equilibrium as expressed by the classical expression for the equilibrium constant has been discussed in detail elsewhere.[4] In summary, it was deduced from the collected experimental evidence that the classical expression for the equilibrium constant was valid for conditions of association under the assumption of no preference in association, *i.e.*, statistical scrambling, of aryl or alkyl groups among the possible aggregate compositions.

The postulate that no preference in association is prevailing does not necessitate that the exchange involves the monomeric species the concentration of which appears in the expression for the equilibrium constant. That the experimentally observed equilibrium concentrations (K_{obsd}) give reasonable constancy, with varying initial concentrations, in the classical expression for the equilibrium constant is an indication that such constants reflect the carbanion stabilities independent of degree of self-association or association with lithium halide.

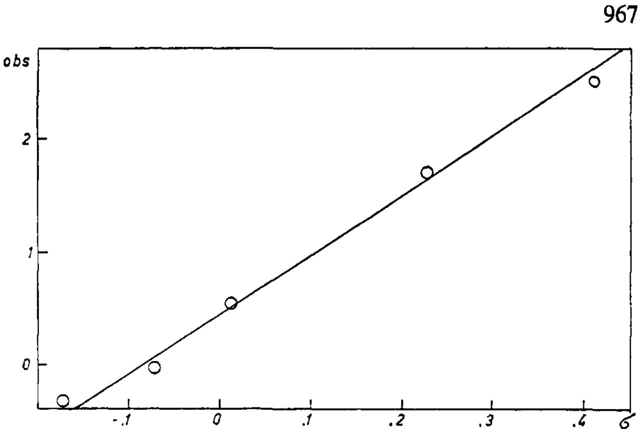

Figure 2. Dependence between substituent constant σ for Z and K_{obsd} for halogen-metal interconversions between C_6H_5Li and ZC_6H_4Br.

In Table II the equilibrium constants are given for a number of substituted bromobenzene compounds. These represent measures of the carbanion stabilities sought relative to organolithium compounds, under the condition of nonpreferential scrambling of the total number of molecules of organolithium compounds present among possible agglomerates. The relation between the equilibrium constant written in the classical form

$$K_{eq} = [ArLi][Ar'Br]/[Ar'Li][ArBr]$$

and the experimentally found equilibrium K_{obsd} under assumption of random scrambling among dimeric aggregates is $K_{obsd} = K_{eq}(K/K')^{1/2}$ in which K and K' are the dissociation constants between dimeric aggregates and monomeric organolithium reagents.[4] It is seen that the relation between K_{eq} and K_{obsd} is independent of the concentrations of the organolithium reagents. If this were not so, one would expect the K_{obsd} to vary with the observed concentrations of organolithium reagents. It is further proposed[4] that the ratio K/K' is close to 1. This is likely to be so in our case of comparing aryllithium compounds. If this were not so, the equilibrium constants, K_{obsd}, would not reflect directly the carbanion stabilities but be dependent on the dissociation constants K and K'.

The equilibrium constants obtained by substituting the total RLi– and R′Li– concentrations into the expression for K_{obsd} do not vary with initial concentrations (which rules out preferential formation of only nonmixed aggregates[4]), nor do the K_{obsd} values vary significantly between the solvent diethyl ether and tetrahydrofuran although the rates of attaining equilibrium do. Figure 2 demonstrates the easy fit of the equilibrium data to a σ–ρ relationship with a large positive reaction constant ($\rho = 5.5$). The implication of this observation is discussed elsewhere.[2] However, the preferential formation of organolithium compounds containing electron-withdrawing substituents over those containing electron-supplying substituents is consistent with the expected basicities of the corresponding carbanions.[11] In this context a carbanion may be considered as the conjugate base of a carbon acid yielding a bromonium ion rather than a proton.

K_{obsd} does not vary within the temperature range and the error limits of the experiments summarized in

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(11) In using the terminology "carbanions of organolithium compounds" it is not implied that carbanions *per se* are present in solution, but that organolithium compounds may be considered formally to contain a polarized $^{\delta-}C\text{–}Li^{\delta+}$ bond, thus inducing partial carbanion character to the organic "radical."

(12) G. Wittig, F. J. Meyer, and G. Lange, *Ann.*, **571**, 167 (1951).

(13) J. F. Eastham and G. W. Gibson, *J. Am. Chem. Soc.*, **85**, 2171 (1963).

(14) R. Waack and M. A. Doran, *Chem. Ind.* (London), 496 (1964).

Table III. K_{obsd} = 0.56 ± 0.04 and 0.40 ± 0.03 in ether and tetrahydrofuran, respectively. Consequently a very low enthalpy change is involved in the halogen-metal interconversion between phenyllithium and *p*-bromotoluene,[15] ΔH°_{277} = 0.17 ± 0.05 kcal/mole in diethyl ether and ΔH°_{277} = 0.01 ± 0.13 kcal/mole in tetrahydrofuran. The change in entropy for the equilibrium process[15] is likewise small ($\Delta S^\circ_{277} = -0.62 \pm 0.15$ cal/deg mole in diethyl ether and -1.85 ± 0.47 cal/deg mole in tetrahydrofuran). This is reasonable since the reactants and products have very similar structures (C_6H_5Li and *p*-$CH_3C_6H_4Br$ *vs.* C_6H_5Br and *p*-$CH_3C_6H_4Li$). The equilibrium constant, K_{obsd} = 0.56 ± 0.04, indicates that the unsubstituted phenyl anion[11] is slightly preferred over the *p*-tolyl anion as the group attached to the electropositive lithium cation.

Experimental Section

The aryl bromides utilized were purified by fractional distillation at reduced pressure; the purity was checked by gas phase chromatography and refractive indices. **Lithium** used in the preparation of the organolithium compounds was pressed into bands from an electrically heated press. The bands were cut into short strips which were allowed to fall directly into purified and dried ether. **Diethyl ether** used throughout the study was purified by heating over freshly pressed sodium wire until a clear blue solution could be obtained on addition of benzophenone. Samples were freshly distilled from these solutions immediately before use. **Nitrogen** used throughout the study was passed over a prereduced BASF catalyst to remove traces of oxygen and then through various drying tubes for the removal of traces of moisture.

Preparation of Aryllithium Reagents. A. Containing Lithium Halide. Freshly pressed lithium (2.2 g-atoms per mole of total aryl bromide) and a small amount of ether was added to a dry nitrogen filled flask equipped with a stirrer, an addition funnel, and a reflux condenser. The aryl halide was added dropwise in ether solution at such a rate that the reacting mixture boiled briskly. Concentrations of the prepared solutions were kept below 0.8 *M* since it was found that at higher concentrations lithium bromide or phenyllithium–lithium bromide precipitated on cooling to room temperature. After complete addition of the aryl bromide the reaction mixture was boiled for an additional 1–2 hr. The solutions of phenyllithium thus prepared were filtered through a dried glass plug into storage burrets[16] which allowed the ready removal of measured quantities of the reagent under nitrogen. The aryllithium reagents thus prepared could be stored for 1–2 weeks at 4° without significant decomposition.

B. Salt Free. A two-necked Schlenk tube was charged with the diarylmercury compound, freshly pressed lithium bands (weight corresponding to *ca.* 5 g-atoms per mole of diarylmercury), some glass splinters (to scratch the surface of the lithium metal when amalgamated), and sufficient ether to produce *ca.* 1 *M* solutions of the desired aryllithium reagent. The Schlenk tube was sealed under nitrogen and agitated in a shaking device for no less than 36 hr. The progress of the reaction was checked by the disappearance of diarylmercury toward the end of the reaction. The amalgam and the mercury were allowed to settle and the salt-free phenyllithium was decanted through a glass plug into a storage burret.[16] Salt-free phenyllithium could be stored at 4° for only 2–3 days before use, because of the much more rapid reaction with ether.

Diphenylmercury. Commercial samples were purified by recrystallization from petroleum ether (bp 60–80°) and drying under high vacuum at 60°.

Di-*p*-tolylmercury. This compound was synthesized by known procedures[17] from *p*-tolylmercury chloride which was prepared from sodium *p*-toluenesulfinate. The di-*p*-tolylmercury was purified by recrystallization from xylene.

Analysis of Aryllithium Reagents. A 2-ml aliquot of the reagent sample was measured into a predried Schlenk tube containing 0.5–1 ml of ethylene bromide in 2–5 ml of ether. After 5 min the reaction mixture was hydrolyzed and titrated with 0.1 *N* sulfuric acid until a phenolphthalein end point (intermittent vigorous shaking is essential). The number of milliequivalents of base present per milliliters of organolithium reagent constitutes the "rest alkali."

Another 2-ml aliquot was hydrolyzed directly and the total base liberated was determined by titration with standardized acid. The total base (per milliliter of reagent) minus the "rest alkali" (per milliliter of reagent) is a measure of the organolithium reagent present in the reagent.

Reaction of Aryllithium with Trimethylchlorosilane. To an ice-cold solution of 2.2 g (20 mmoles) of trimethylchlorosilane was added 34.2 ml of 0.525 *M* lithium bromide containing phenyllithium (18 mmoles total). The reaction mixture was allowed to heat to room temperature and Color Test I[18] was found to be negative. The reaction mixture was hydrolyzed and the ether layer was dried over calcium sulfate and diluted to 50 ml. To 2-ml of this solution was added a weighed amount (38.5 mg) of internal standard (*m*-xylene), and a vapor phase chromatographic analysis was performed. The remainder of the solution was concentrated and the phenyltrimethylsilane was isolated by distillation: 2.48 g, vapor temperature 101° at 100 mm, $n^{19}\mathrm{D}$ 1.4862 (lit.[19] 1.488), isolated yield 95%. The purified phenyltrimethylsilane was used for the determination of the response factor in relation to *m*-xylene. The vpc yield was calculated by using this response factor and the integrated areas of the vapor phase chromatogram of the ether solution of the reaction mixture to which the internal standard had been added. The vpc yield was 102% based on the double titration, which is often low by 2–4%.

A similar experiment with *p*-tolyllithium gave an isolated yield of *p*-tolyltrimethylsilane of 2.43 g, 86%, vpc yield 104%, again indicating that the double titration is low.

Interconversion between Phenyllithium and *p*-Bromotoluene. Example. The reaction vessel was dried and filled with nitrogen and then heated in a constant temperature bath to 25 ± 0.1°. It was charged with 1.041 g (6.090 mmoles) of *p*-bromotoluene, 4.25 ml of ether, and 15.0 ml of 0.82 *M* phenyllithium (12.3 mmoles), prepared by method A. At desired intervals 1-ml samples were removed by means of a 1-ml pipet oven dried at 140° and cooled in a rapid nitrogen stream. The aliquots were added to a mixture of 80 μl of chlorotrimethylsilane and a weighed amount of internal standard (*m*-xylene). A precision syringe preset to deliver a given weight of *m*-xylene (40.98 mg) was used in order that identical weights of internal standard could be delivered conveniently to each aliquot of reaction sample removed. The reaction with trimethylchlorosilane went to completion within 1 min, and after 5 min of standing at room temperature, a complete vpc analysis was performed. Samples were removed every 30 min for 6–8 hr and then after *ca.* 24 hr to obtain the equilibrium position.

Vapor Phase Chromatographic Analyses. Suitable conditions for the desired analyses were found to be: F & M Model 720 instrument, dual-column programmed temperature vapor chromatograph, analytical column (6-ft 10% silicone rubber, SE-30 on 60–80 P), reference column (same packing, 2 ft), injection temperature 285°, detector temperature 350°. Column temperature was 75° until after internal standard had been eluted, then programmed 20°/min until oven temperature reached 250°. For the purpose of determining the response factors, mixtures of the relevant substances were weighed out and analyzed under the standard conditions. The peak areas were measured by a Honeywell disk integrator. The response factors determined from various vapor phase chromatograms and different mixtures varied from the average by less than 2% and changed by less than 1% over a period of 6 months, using the same column.

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(15) From the definition of the free-energy change of an equilibrium process and assuming $\Delta C_p = 0$, $\Delta G^\circ_T = \Delta H^\circ_T - T\Delta S^\circ_T$ (the superscripts indicating unit activities, *T* being the mean temperature) one obtains $\Delta G^\circ_T/T = \Delta H^\circ_T/T - \Delta S^\circ_T$. The reaction isotherm, $\Delta G^\circ_T = -RT \ln K$, yields $\Delta G^\circ_T/T = -2.303R \log K$, which combined with the expression for $\Delta G^\circ_T/T$ produces $-2.303R \log K = \Delta H^\circ_T/T - \Delta S^\circ_T$. Thus plotting $+2.303R \log K$ against $1/T$ one would expect a line having a slope of $-\Delta H^\circ_T$ and an intercept of ΔS°_T. The error limits given throughout are the standard deviations derived from a least-squares treatent of the data without weighing the points.

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Stoichiometry of Reaction. For all reactions shown in Tables I–III the molarities of the reactants as well as the products were calculated. In addition the molarities of benzene, toluene, biphenyl, di-*p*-tolyl, and 4-methylbiphenyl could be estimated. It was established that for the concentration ranges and temperatures used, the rates of the possible side reactions were too slow to interfere with the rate of halogen–metal interconversion.

Mechanism of Halogen–Metal Interconversion between Aryl Bromides and Aryllithium Compounds. II. Rate Studies

Hans J. S. Winkler and H. Winkler

Contribution from Monsanto Research SA, Zürich, Switzerland.
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Abstract: The rates of halogen–metal interconversions between a number of aryllithium compounds and substituted aryl bromides have been measured. Agreement between rate data and equilibrium data for these processes coupled with observations of a salt effect, activation parameters, and solvent effects are discussed relative to the reaction mechanism.

It has not been until recently that rate studies involving organolithium compounds have been reported. One of the difficulties encountered is the complexity of the organolithium species present in solution. This often makes interpretation of rate data subject to an array of assumptions which obscures the significant details of the rate-determining steps.

Halogen–metal interconversions generally have been considered to be extremely fast reactions.[1] This is true of most interconversions and in general the rate decreases along the series I > Br > Cl >> F. More recently the dependence of rate on medium has been demonstrated.[2] It has even been shown that the course of a reaction between an organolithium compound and a halide can be altered by the use of a different solvent.[3]

A study of the solvent effect[4] showed that ethereal solvents have a pronounced effect on the rate-determining consumption of butyllithium in the coupling with 1-bromooctane. The observation that better ion-solvating solvents favor halogen–metal interconversions even of Grignard reagents has recently been published.[5]

In our previous publication[6] it was concluded that halogen–metal interconversions between phenyllithium and aryl bromides were equilibrium processes. The extension of this work deals with a study of the rate processes involved.

Results

It was found that halogen–metal interconversions between aryllithium compounds and aryl bromides in ether proceed at rates convenient for kinetic studies at room temperature. Such systems, furthermore, would be convenient for study because the electronic effects of substituents on the arene nuclei have been systematized.

$$\mathrm{ArLi} + \mathrm{Ar'Br} \rightleftharpoons \mathrm{ArBr} + \mathrm{Ar'Li}$$

The techniques used in measuring the rates are described in the first publication of this series.[6] For all reactions mentioned in this study the concentrations of reactants as well as products were estimated at every kinetic point. This was done partly to eliminate possibilities of the side reactions discussed elsewhere[6] and partly to ascertain that the rates measured were indeed the rates of interconversion. The side reaction involving benzyne intermediates has been studied by the rate of lithium halide liberated.[7] From this study it is evident that only for fluoro substituents is the elimination–addition reaction competitive with halogen–metal interconversion.

Table I summarizes the rate data measured for the halogen–metal interconversions between salt-containing phenyllithium and some substituted aryl bromides. The rate constants were evaluated graphically by substituting the concentration *vs.* time data into second-order integrated rate expressions. The data are depicted in Figure 1 showing fair linear agreement between the σ constants for the substituents and log k. From the slope of this line the reaction constant ρ was evaluated to be 4.0.

It was found that the halogen–metal interconversion adhered to second-order rate laws. Table II summarizes the apparent agreement between the independently determined rate constants k_+ and k_- and K_{obsd} found by substitution of equilibrium concentrations. The table also shows that the same results are found for salt-free as for salt-containing aryllithium reagents. This indicates that the equilibrium constant in both cases is dependent on the carbanion stabilities despite differences in mechanisms expected.

Salt Effects. There are indications[8] that salt-free and salt-containing aryllithium compounds are present

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