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NOTE

THE HALOGEN-METAL INTERCONVERSION OF ARYL BROMIDES AND n-BUTYLLITHIUM IN NON-POLAR SOLVENTS

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The halogen-metal interconversion reaction is a general and widely accepted method for the preparation of aryllithium compounds[1]. Ethereal solvents usually are employed because of the ease of reaction and solubility of the reactants and end products; however, the halogen-metal interconversion also has been carried out to good advantage in non-polar solvents such as benzene[2,3], cyclohexane[2] and pentane[4-7]. Although the interconversion probably involves equilibrium conditions[8], the reaction of an aryl halide and an alkyllithium in non-polar solvents proceeds essentially to completion because of the relatively low solubility of the aryllithium produced.

In this study, the reaction times necessary to produce aryllithium compounds in a variety of non-polar solvents were determined by following the consumption of n-butyllithium.

EXPERIMENTAL PROCEDURE

Commercial n-butyllithium (0.02 mole) in hydrocarbon solvent was added rapidly by syringe to hydrocarbon (115 ml) solutions of aryl bromides (0.02 mole) in 7 oz. soft glass bottles closed with self-sealing rubber gaskets and perforated crown caps. The bottles were agitated in a constant temperature bath. Five-ml samples were periodically removed by syringe and hydrolyzed in sealed Diels-Alder tubes containing one ml of ethanol and 0.25 mmole of isobutane as an internal standard. A 500 μl sample of the gas phase was analyzed isothermally by use of a 20-foot HMPA gas chromatograph column.

For complete product analyses, aliquots were removed and hydrolyzed as described above. The liquid phase was analyzed on a 10-foot Apiezon column programmed at 7.9°/min.

RESULTS AND DISCUSSION

The results of the halogen-metal interconversion reaction of n-butyllithium and several aryl bromides are summarized in Table 1. Subsequent to complete n-

TABLE 1

REACTION TIME OF HALOGEN–METAL INTERCONVERSION AS DETERMINED BY BUTYLLITHIUM CONSUMPTION

Aryl halide	RLi[a]	Solvent	Temp. (°C)	Time[b] (min)
Bromobenzene	n-Butyl	Toluene	50	300
1,4-Dibromobenzene	n-Butyl	Toluene	50	95
1,3-Dibromobenzene	n-Butyl	Toluene	50	30
1,2-Dibromobenzene	n-Butyl	Toluene	50	[c]
1,3-Dibromobenzene	n-Butyl	Hexane	50	80
1,3-Dibromobenzene	n-Butyl	Cyclohexane	50	70
1,3-Dibromobenzene	n-Butyl	Toluene	50	30
1,3-Dibromobenzene	n-Butyl	Toluene	5	1800
1,3-Dibromobenzene	n-Butyl	Toluene	30	120
1,3-Dibromobenzene	n-Butyl	Toluene	50	30
Bromobenzene	sec-Butyl	Toluene	50	[c]
1,3-Dibromobenzene	sec-Butyl	Toluene	50	[c]
1,3-Dibromobenzene	sec-Butyl	Toluene	5	[c]
1,3-Dibromobenzene	n-Butyl	Diethyl ether	5	[c]
1,4-Dibromobenzene	n-Butyl	Diethyl ether	5	[c]

[a] Molar equivalent. [b] Time to total butyllithium consumption. [c] Butyllithium consumed before a sample could be withdrawn (<30 sec).

TABLE 2

PER CENT HALOGEN–METAL INTERCONVERSION DETERMINED BY ACID TITRATION OF THE HYDROLYZED REACTION PRODUCT

Aryl halide	RLi[a]	Solvent	% Conversion[b] at		
			50°	30°	5°
Bromobenzene	n-Butyl-	Toluene	95		
Bromobenzene	sec-Butyl-	Toluene	75		
1,4-Dibromobenzene	n-Butyl-	Toluene	82		
1,4-Dibromobenzene	n-Butyl-	Diethyl ether			90
1,3-Dibromobenzene	n-Butyl	Toluene	92	90	87
1,3-Dibromobenzene	n-Butyl-	Cyclohexane	81		
1,3-Dibromobenzene	n-Butyl-	Hexane	71		
1,3-Dibromobenzene	n-Butyl	Diethyl ether			97
1,3-Dibromobenzene	sec-Butyl-	Toluene			100
1,2-Dibromobenzene	n-Butyl-	Toluene	0		

[a] Molar equivalent. [b] Per cent alkalinity determined by acid titration of a hydrolyzed aliquot following complete consumption of n-butyllithium.

butyllithium consumption, conversion to aryllithium was determined by acid titration of hydrolyzed aliquots. These results are summarized in Table 2.

The presence of a second halogen on the ring accelerated the exchange reaction. Bromophenyllithiums were the resulting products. Interestingly, the halogen–metal interconversion reaction was more rapid with 1,3-dibromobenzene than with 1,4-dibromobenzene. The exchange reaction should be expedited by an increase in the positive character of the halogen involved in the halogen–metal interconversion reaction. The Hammett[9] σ value for a *para* bromine substituent is $+0.232$ and is $+0.391$ for the *meta* substituent. Thus, the increasing electron-withdrawing power of these substituents follows the observed order of reactivity. Reaction with 1,2-dibromobenzene, presumably giving the benzyne intermediate, was too rapid to follow by this technique.

The relative rates of n-butyllithium consumption (up to 60%) with 1,3-dibromobenzene, 1,4-dibromobenzene and bromobenzene were 10/2/1, respectively. Reaction rates decreased as the level of n-butyllithium reached a lower concentration.

The physical apprearances of the organometallic products also were strikingly different. Phenyllithium and 4-bromophenyllithium appeared to be composed of large agglomerates (10–27 μ) that settled in a matter of minutes upon standing. In contrast, 3-bromophenyllithium was finely divided ($< 1\ \mu$) and remained in suspension for over an hour. The agglomerate particle size was influenced by the rate of agitation during the halogen–metal interconversion reaction and was decreased by increased physical agitation. Attrition of the agglomerates also gave smaller particle size and increased activity of the organometallic products.

The relatively small particle size of 3-bromophenyllithium compared to phenyllithium or 4-bromophenyllithium made this compound the easiest to investigate. Accordingly, the effect of solvent and temperature were studied in the reaction of n-butyllithium and 1,3-dibromobenzene. The relative rates of n-butyllithium consumption (up to 60%) in toluene, cyclohexane and n-hexane were 6/1.5/1, respectively. The product particle size increased in the reverse order ($< 1\ \mu$, 4–40 μ, and 7–80 μ; respectively). The rate of the halogen–metal interconversion reaction became impractically slow at 5°, and the relative rates of n-butyllithium consumption at 50°, 30° and 5° were 56/10/1. Product particle size increased at the lower temperatures.

The reactivity of the aryllithium appeared to be dependent on the product particle size. 3-Bromophenyllithium prepared in toluene cleaved *p*-tolyldisulfide in less than five minutes in the disulfide cleavage method for organolithium analysis[10]. In contrast, disulfide cleavage by 3-bromophenyllithium prepared in hexane was negligible after one hour. Replacement of the original solvent used in the exchange reaction by another non-polar solvent did not have a significant effect on the reactivity of the organometallic product.

Secondary coupling reactions of n-butyllithium and n-butyl bromide were not extensive as the halogen–metal interconversion reactions gave high yields of alkalinity after the n-butyllithium had been consumed (Table 2). A complete product analysis was carried out on the hydrolyzed products of the n-butyllithium and 1,3-dibromobenzene reaction in which all but 16.7% of the dibromide had been consumed. The amount of bromobenzene, the hydrolysis product of 3-bromophenyllithium, was less than indicated by titration. Possibly, halogen–metal interconversion with the second bromine giving 1,3-dilithiobenzene was a competing reaction, and it is to be noted that carbonation of a 3-bromophenyllithium preparation gave a small amount of isophthalic acid in addition to 3-bromobenzoic acid. The complex solvent of the commercial n-butyllithium interfered with the identification of benzene, the hydrolysis product of the dilithium compound. The amount of n-butyl bromide found was approximately equivalent to the original n-butyllithium charge and indicates that an interfering coupling reaction was insignificant. Also, n-octane was not found in the reaction products.

Substitution of sec-butyllithium for n-butyllithium in the reaction of 1,3-dibromobenzene or bromobenzene in toluene resulted in a halogen–metal interconversion too rapid to measure by this technique. It is interesting to note that good conversion as determined by titration of the hydrolyzed product was obtained (Table 2). Furthermore, good conversion also was obtained in the reaction of n-butyllithium and either 1,3-dibromobenzene or 1,4-dibromobenzene in diethyl ether at 5° even though the reaction was too rapid to follow. The respective acids, 3-bromobenzoic acid (79.8% pure yield) and 4-bromobenzoic acid (61.6% pure yield), were isolated as proof of identity.

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