Notes A department for short papers of immediate interest.

Effect of Sodium in the Preparation of Organolithium Compounds

CONRAD W. KAMIENSKI AND DONALD L. ESMAY

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The sodium content of the lithium metal has been reported recently to affect the ease of preparation of *p*-dimethylaminophenyllithium,[1] of *tert*-butyllithium,[2] and of *n*-butyllithium[3] by the metal-

$$RX + 2Li \longrightarrow RLi + LiX \qquad (1)$$

organic halide reaction (1). These observations prompt us to report some results we have obtained in this connection. While the most striking effects have been observed by us in preparations of *p*-dimethylaminophenyllithium and *tert*-butyllithium, we have also determined that the ease of preparation of *n*-butyllithium and phenyllithium is affected to some extent by the sodium content of the lithium metal

In our hands, lithium metal containing less than 0.005% sodium[4] could not be made to react at all with *p*-bromodimethylaniline in ethyl ether. Excellent yields (over 95%) of *p*-dimethylaminophenyllithium were obtained when either lithium wire or lithium ribbon containing about 0.02% sodium[5] was treated with *p*-bromodimethylaniline in ethyl ether.

In comparative reactions of the two grades of lithium metal with bromobenzene and with *n*-butyl bromide in diethyl ether, the differences in yields were considered significant for *n*-butyllithium (15% or greater) but not for phenyllithium (less than 10%). In both cases the physical appearances and, to a lesser extent, the rate of the reactions were affected by the amount of sodium present in the lithium metal. The best over-all preparations of phenyllithium and *n*-butyllithium were obtained using the lithium metal containing about 0.02% sodium.[5]

The ease of preparation of organolithium compounds in hydrocarbon solvents has also been found by us to be related to the sodium content of the lithium metal used. For example, we have been able to prepare *tert*-butyllithium in pentane consistently in yields over 80% provided that we use a dispersion prepared from lithium metal containing 2% sodium.

We do not know at this time the critical or optimum concentration of sodium in the lithium metal that is necessary to ensure that a satisfactory organolithium preparation can be made. Preliminary results indicate that this concentration varies with the organic halide substrate used. Additional studies are being carried out.

EXPERIMENTAL

p-Dimethylaminophenyllithium. A. In a 250-ml., three necked, round bottomed flask, equipped with mechanical stirrer, reflux condenser, and dropping funnel (the latter two fitted with gas inlets for argon), was placed 1.2 g. of finely cut lithium metal ribbon ("regular"[5] grade) and 50 ml. of anhydrous ethyl ether. The lithium metal was cut directly into the flask in an exit flow of argon to keep the cut surface shiny. To the stirred suspension in the flask was added, *all at once*, 3–4 ml. of a solution of 15.6 g. (0.078 mole) of *p*-bromodimethylaniline[6] in 60 ml. of ether. On heating the mixture to reflux the reaction was initiated after about 5 to 10 min. time as evidenced by a reddish brown coloration of the suspension and pitting of the metal surface. The remainder of the solution was added over a 1-hr. period with refluxing evidenced throughout. Stirring and refluxing were then continued over a 3-hr. period with a gradual brightening and disappearance of the metal. After allowing the mixture to cool, the contents of the flask were filtered through a glass wool plug (under argon) into a 100-ml. graduated dropping funnel (total volume, 101 ml.). A 2-ml. aliquot of the clear supernatant liquid was taken, hydrolyzed, and titrated with standard acid, using thymol blue as indicator (yield, 97%). The remaining solution in the dropping funnel was carbonated by gradual addition to a Dry Ice–ether slurry. The crude yield of *p*-dimethylaminobenzoic acid (m.p. 200°, lit., m.p. 240–241°) obtained after work-up was 65%.

B. This was a duplicate of Run A except that "low sodium"[4] lithium metal was used. No reaction was observed even on prolonged refluxing and stirring after addition of the total amount of *p*-bromodimethylaniline. When small chips of "regular"[5] grade lithium metal were added to this mixture immediate, vigorous reaction with these chips was observed. However, reaction ceased as soon as the chips were used up.

C. This was a duplicate of Run A except that lithium wire was used. Results were essentially identical with those of Run A.

tert-Butyllithium. In a 1-l., three necked, round bottomed flask, equipped with mechanical stirrer, reflux condenser, and dropping funnel (the latter two fitted with gas inlets for argon) was placed 120 g. of lithium dispersion [15% in a petrolatum (20%)-mineral oil (65%) mixture] and 200 ml. of dry, "unsaturate-free"[7] *n*-pentane. The lithium metal

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[1] J. B. Wright and E. S. Gutsell, *J. Am. Chem. Soc.*, **81**, 5193 (1959), ref. 10.

[2] M. Stiles and R. P. Mayer, *J. Am. Chem. Soc.*, **81**, 1497 (1959) ref. 38b.

[3] J. A. Beel, W. G. Koch, G. E. Tomasi, D. E. Hermansen, and P. Fleetwood, *J. Org. Chem.*, **24**, 2036 (1959).

[4] Lithium Corp. of America "low-sodium" grade lithium.

[5] Lithium Corp. of America "regular" grade lithium as currently produced.

[6] The *p*-bromodimethylaniline used in these runs was Eastman Kodak's practical grade which was recrystallized once from Synasol before use (m.p. 53–55°, lit. m.p., 55°).

contained 2% of sodium. The mixture was stirred and heated to reflux. The dropwise addition of a solution of 92.6 g. (1.0 mole) of *tert*-butyl chloride[8] in 250 ml. of dry "unsaturate-free" *n*-pentane was then begun. After addition of about 5 ml. of the halide solution, the rate of reflux increased appreciably and the source of heat was removed. The remainder of the halide solution was then added over a 2.5-hr. period, at a rate such that sustained reflux was maintained throughout the addition. The reaction mixture was stirred for 0.5 hr. longer. The product solution was then filtered away from the residue of lithium chloride and excess metal through a sintered glass filter tube,[9] into a graduated dropping funnel (total volume, 589 ml.). Three-milliliter aliquots of the clear solution were then taken, hydrolyzed in flasks containing 10 ml. of standard 0.5*N* acid, and back-titrated with standard 0.1*N* base to a phenolphthalein end point. The yield of *tert*-butyllithium (based on *tert*-butyl chloride) was 89%.

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LITHIUM CORP. OF AMERICA, INC.
MINNEAPOLIS 16, MINN.

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[7] The *n*-pentane was a 99 mole % (Phillips "Pure") grade which had been stirred with concd. sulfuric acid for 3 days, separated, washed with 5% sodium bicarbonate solution, washed with water, dried over calcium chloride (anhyd.) and, finally, dried over sodium ribbon.

[8] The *tert*-butyl chloride was obtained from Matheson, Coleman and Bell (purified grade); b.p. 51–52°, n_D^{20}, 1.3851.

[9] Ace Glass Co., Cat. No. 8575—porosity "E."

The Preparation of Grignard Reagents under Helium and Argon

F. H. OWENS, R. P. FELLMANN, AND F. E. ZIMMERMAN

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Grignard reagents prepared by conventional methods generally contain excess magnesium halide arising from a Wurtz-type reaction (Equation 1), and various preparative methods have been used to avoid this undesirable reaction.[1] Several investigators[2] have shown that the course of a Grignard

$$2RX + Mg \longrightarrow R{-}R + MgX_2 \qquad (1)$$

reaction can be altered by varying the amount of magnesium halide.

Recently we have found that the preparation of Grignard reagents under helium or argon, rather than the customary nitrogen or ether, consistently leads to higher yields and to smaller amounts of coupling products. The Grignard reagents listed in Table I were prepared by the dropwise addition of the organic halide to a 10% excess of magnesium metal in ether. The Grignard reagents prepared under helium or argon were clear, almost colorless solutions while those prepared under nitrogen or ether were cloudy, dark-colored solutions. One-milliliter samples were titrated with hydrochloric acid and with silver nitrate to determine the amount of excess halide. The values shown represent the average of several experiments in which the reproducibility was excellent.

TABLE I

GRIGNARD REAGENTS PREPARED UNDER HELIUM, ARGON, NITROGEN, AND ETHER

Halide	Prepared under	Yield,[a] %	Excess Halide,[b] %
n-Butyl chloride	Helium	99.0	0.0
n-Butyl chloride	Nitrogen	91.0	2.2
n-Butyl bromide	Helium	97.5	1.1
n-Butyl bromide	Argon	97.8	1.0
n-Butyl bromide	Nitrogen	80.1	15.2
n-Butyl bromide	Ether	89.0	7.7
Cyclohexyl bromide	Helium	68.3	38.5
Cyclohexyl bromide	Nitrogen	30.5	75.4
Bromobenzene	Helium	99.0	0.0
Bromobenzene	Argon	95.2	2.1
Bromobenzene	Nitrogen	85.0	8.0
Bromobenzene	Ether	88.3	5.7
Iodobenzene	Helium	81.0	10.2
Iodobenzene	Nitrogen	70.4	16.5
Benzyl bromide	Helium	91.3	7.6
Benzyl bromide	Nitrogen	62.2	20.3
Benzyl bromide	Ether	53.0	25.8

[a] Based on the acid titration. [b] The per cent excess halide is the quotient of the difference between the total base and halide titrations and the total base titration.

The principal advantages which accrue from this method are that (1) purification of the purging gas is unnecessary; (2) higher yields of the Grignard reagent are obtained; and (3) there is little or no contamination by coupling products. Furthermore, dilution of the halide with ether is not required so that concentrated solutions of the Grignard reagent are obtainable, and only 10% excess magnesium is used as compared with the one- to three-mole excess used in some preparations.[1]

EXPERIMENTAL

Magnesium. Domal High Purity, sublimed magnesium granules (Dominion Magnesium Co., Ltd., Haley, Ont.) was used.

Diethyl ether. Mallinckrodt analytical reagent ether containing 5×10^{-6} % sodium diethyldithiocarbamate was used without further treatment.

Organic halides were obtained from Distillation Products Industries and were dried over calcium chloride prior to use.

Nitrogen. Prepurified grade (Air Reduction Sales Co.) containing less than 0.002% oxygen and 0.0012% water was used without further treatment.

Helium was obtained from the Matheson Co., Inc. Minimum purity, 99.99%, used without further treatment.

Argon, obtained from the Matheson Co., Inc. Minimum purity, 99.998%, was used without further treatment.

Preparation of the Grignard reagents. The apparatus consisted of a three necked, round bottom flask equipped with a Dry Ice reflux condenser attached to a mercury bubbler,

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[1] M. S. Kharasch and O. Reinmuth, *Grignard Reactions of Nonmetallic Substances,* Prentice-Hall, Inc., New York, 1954, Chap. II.

[2] C. G. Swain and H. B. Boyles, *J. Am. Chem. Soc.,* **73**, 871 (1951); E. T. McBee, O. R. Pierce, and J. F. Higgins, *J. Am. Chem. Soc.,* **74**, 1736 (1952); A. C. Cope, *J. Am. Chem. Soc.,* **56**, 1578 (1934); R. C. Huston and A. H. Agett, *J. Org. Chem.,* **6**, 123 (1941).