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A METHOD FOR ACCURATE TITRATION OF ALKYLLITHIUM REAGENTS IN ETHER SOLUTIONS

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SUMMARY

Accurate and precise concentrations of n-butyllithium in solutions of hexane in various ethers have been determined by direct titration at −78° with sec-butanol.[4]

In connection with other studies on the chemistry and stability of alkyllithiums, we found it desirable to be able to easily and rapidly determine the concentrations of these reagents in ethers. This has previously been difficult due to the ready mutual destruction[1] of ethers and alkyllithiums. The speed of this decomposition is a function of the structures of both the ether and the alkyllithium and some preliminary mechanistic speculation exists[2,3]. We assumed that this decomposition would be sufficiently quenched at low temperatures to permit reasonable analysis. In fact, accurate and precise values can be obtained by working at −78° using the sec-butanol, 2,2′-biquinoline system of Watson and Eastham[4].

EXPERIMENTAL

Materials and Equipment. n-Butyllithium in hexane solution was obtained from Alfa Inorganics Inc., the concentration being listed as 22%. The 1,2-dibromoethane used in the Gilman double titration was dried over phosphorus pentoxide for 12 h, decanted and distilled at atmospheric pressure. The various ethers were dried by refluxing over and then distilling from lithium aluminum hydride. They were stored under argon and over molecular sieves (4A) previously activated by heating under reduced vacuum (1 mmHg). The 2,2′-biquinoline was used directly as supplied by Aldrich Chemicals as a 0.13% solution in dry xylene. Both hexane and xylene were obtained initially from freshly opened bottles and subsequently stored over activated molecular sieves. sec-Butanol was refluxed 16 h over lithium aluminum hydride, distilled and stored under argon and over activated molecular sieves. The hydrochloric acid used in the Gilman procedure was standard 1.0 *N* obtained from Fisher Scientific Co. The syringes were standard, the B–D Yale type with a reading error estimated conservatively at ±0.03 ml. Before use they were oven-dried at 110° for 2–6 h and then stored in a dessicator over phosphorus pentoxide. Other glassware was

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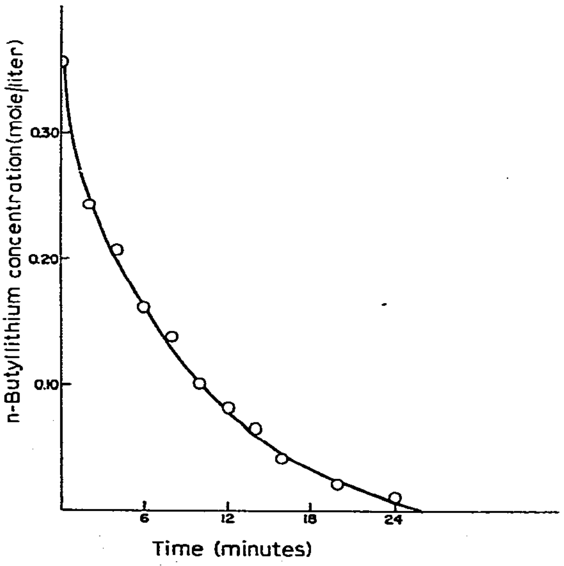
dried by Bunsen flame under a flow of argon. The error in reading the burette was estimated to be ±0.03 ml.

General titration procedure. A reservoir of n-butyllithium in hexane was prepared by diluting the commercial reagent (6.1 ml) with dry hexane (35 ml), resulting in a solution approximately 0.37 *M*. During the course of the experiment, the solution was kept at room temperature in a dry flask fitted with a septum and an argon atmosphere. The titrating vessel consisted of a dry, three-neck flask fitted with septums, teflon stirring bar and a balloon reservoir to maintain a positive pressure of argon. The standard solution of sec-butanol in xylene (1.013 *M*) was delivered to the flask from a 10 ml burette which was also pre-dried and fitted with an argon balloon reservoir, the tip being inserted through the center septum with a tight seal. For titrations, the flask was charged with solvent (8–10 ml), followed by 2,2′-biquinoline solution (12–14 drops) and then permitted to equilibrate to −78° for 5 min. An aliquot of n-butyllithium solution (2.0 ml) was removed from the reservoir, injected into the vessel and titrated with rapid stirring. In the presence of n-butyllithium, the indicator developed a light yellow color. As the titration approached equivalence, the solution developed a pale violet tinge. The end point was taken as the point at which the solution became almost colorless. Addition of a second aliquot regenerated the indicator color and a second titration was carried out as above.

1,2-Dimethoxyethane (DME) decomposition study. The titrating vessel at −78° was charged with hexane (0.6 ml), DME (9.0 ml) and a few drops of 2,2′-biquinoline indicator solution. To a dry, three-neck flask at 0° containing dry DME (20 ml) was added a solution of n-butyllithium in hexane (3.10 ml). The temperature was kept constant with a Lauda circulator connected to a Haake heat exchanger. A preliminary titration was made on 0.5 ml to ensure dry conditions. Then, periodically, aliquots



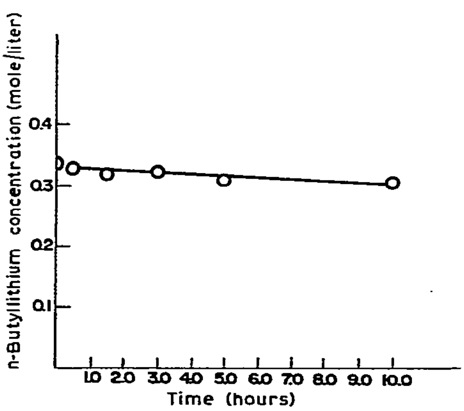


Fig. 1. Decomposition of n-butyllithium in 1,2-dimethoxyethane at 0°.

Fig. 2. Decomposition of n-butyllithium in tetrahydrofuran at −78°.

were removed from the reaction flask and titrated according to the above procedure. The results are shown in Fig. 1.

Tetrahydrofuran decomposition. A solution of n-butyllithium in hexane (3.17 ml) in dry tetrahydrofuran at −78° was made and titrated in a manner identical to that above. The results are shown in Fig. 2.

RESULTS AND DISCUSSION

The classical Gilman double titration procedure for alkyllithiums[6] has been recently superseded by the more direct titrations using either benzoic acid[7] or sec-butanol[4] as standard acid. However, for monitoring the concentrations of rapidly decomposing solutions they are still unsatisfactory*. A seemingly practical but as yet unapplied solution was to effectively quench this reaction by working at low temperatures. For this technique to be effective it is clear that certain conditions must obtain: (1) at the lower temperature the neutralization must still be rapid, (2) the ether solvents must not interfere with the alkyllithium, alkyllithium–indicator complex equilibrium, (3) reagent decomposition must indeed be slow relative to the titration time interval, (4) optimally the solution should remain homogeneous throughout the titration and (5) in determining concentrations of systems at temperatures less than ambient, systematic errors due to solution warming during transfer must be minimal.

At −78° the dimethyl sulfoxide–monoglyme–hexane solution of Eppley and Dickson[7] solidified during addition and was examined no further. The sec-butanol–xylene system of Watson and Eastham proved acceptable and was used in all runs. Table 1 records the results of titrations of aliquots of a reservoir solution of n-butyllithium in hexane without ether present. No substantial changes were noted at the lower temperature except that the end-point became somewhat more sluggish and was approached with caution. The solution remained homogeneous. We found our values to be consistently higher than those obtained by the Gilman procedure and ascribe the slight difference between the values for the two indicators to a matter of

TABLE 1

TITRATION OF n-BUTYLLITHIUM IN HEXANE

A solution of n-butyllithium in hexane was analyzed at room temperature by both the double titration and direct titration procedures and at −78° by the latter. Aliquots were added and titrated consecutively using the same initial volume of hexane.

	Mean[a]	*Sm*[b]	*n*[c]	Temperature
Double titration[d]	0.330	—	2	r.t.
Direct titration[e]	0.345[f]	0.004	4	r.t.
Direct titration[e]	0.339[g]	0.001	3	r.t.
Direct titration[e]	0.345[g]	0.008	5	−78°

[a] Concentration in moles per liter. [b]. Standard deviation of the mean. [c]. Number of determinations. [d] Ref. 6, [e] Ref. 4. [f] 1,10-Phenanthroline as indicator. [g] 2,2′-Biquinoline as indicator.

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* These decompositions can be extremely rapid. For example, addition of 1.5 *M* n-butyllithium in hexane to 1,2-dimethoxyethane at room temperature resulted in a rapid, exothermic reaction with deposition of a white precipitate[5].

end-point definition. 2,2′-Biquinoline gave more clearly visible end-points and was used in all subsequent runs. After titration of one aliquot, addition of a second aliquot regenerated the indicator color and the newly added lithium reagent could be cleanly titrated. Using this technique, we were able to titrate as many as ten consecutive aliquots without disrupting the titration assembly.

TABLE 2

TITRATIONS OF n-BUTYLLITHIUM IN ETHERS

Aliquots of n-butyllithium in hexane were added to ethers at −78° and analyzed by the direct titration method[a]. The values for each ether determination were compared against the hexane concentration for that run by titration of the hexane solution at room temperature. The indicator was 2,2′-biquinoline. Aliquots were added and titrated consecutively using the same initial volume of ether.

Solvent	−78°			25°[b]		
	Mean[c]	*Sm*[d]	*n*[e]	Mean	*Sm*	*n*
$(C_2H_5)_2O$	0.350	0.003	6	0.346	0.002	3
THF	0.330	0.001	3	0.330	0.002	3
DME[f]	0.338	0.002	4	0.340	0.003	3
DME/TMEDA[g]	0.352	0.003	6	0.343	0.006	8

[a] Ref. 4. [b] Titration of hexane resevoir solution. [c] Concentration in moles per liter. [d] Standard deviation of the mean. [e] Number of determinations. [f] 1,2-Dimethoxyethane. [g] Tetramethylethylenediamine.

Table 2 gives the results of titrations conducted in the presence of various ethers. For each ether, aliquots were drawn from a reservoir of n-butyllithium in hexane at room temperature and added to a volume of ether at −78°. The values obtained for the ether solutions were compared to those obtained for the reservoir itself (titration at room temperature without ether) and were in good agreement. At −78°, 1,2-dimethoxyethane (DME) solidified but titrations could be effected by dilution with hexane to a hexane–DME ratio of 1/15. Dioxane also solidified at this temperature but did not respond to dilution until impractical volumes were reached. Because of the strong complexing ability of tetramethylethylenediamine (TMEDA) with alkyllithiums[8] and its increasing use in synthesis, we examined its response and found such solutions to be readily titrated.

To demonstrate the utility of this technique, we established solutions of n-butyllithium in hexane–ether solutions at different temperatures and followed the decomposition with time. The results of two runs are given in Figs. 1 and 2 and show that decomposition is effectively quenched at −78° and that good results may be obtained under conditions of rapid reaction. We made no specific attempt to determine the lowest concentration titratable under these conditions. However, from Fig. 1, the last point represents a reservoir concentration of 0.01 *M*. Translating this value to the actual concentration in the titrating flask, this amounts to facile analysis of a $6.7 \cdot 10^{-4}$ *M* solution.

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