

A CONVENIENT METHOD FOR THE ACCURATE ESTIMATION OF CONCENTRATIONS OF ALKYL LITHIUM REAGENTS

MICHAEL F. LIPTON*, CHARLES M. SORENSEN, ALAN C. SADLER

Department of Chemistry, Michigan State University, East Lansing, Michigan 48824 (U.S.A.)

and ROBERT H. SHAPIRO

Department of Chemistry, University of Colorado, Boulder, Colorado 80309 (U.S.A.)

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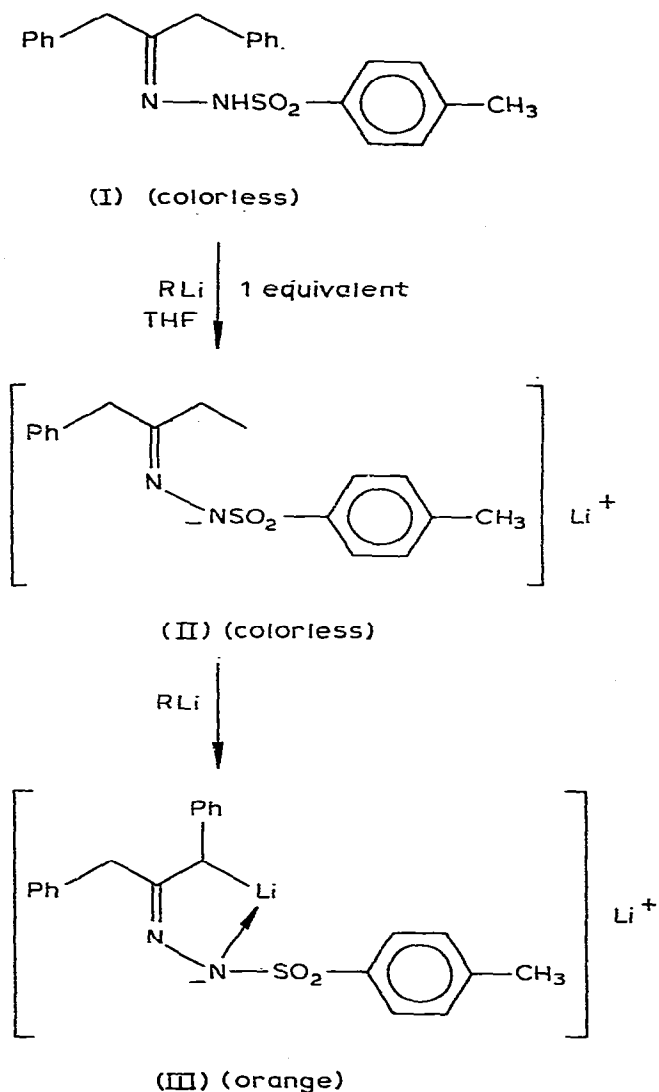
Summary

1,3-Diphenyl-2-propanone tosylhydrazone in tetrahydrofuran solvent is shown to be an effective reagent for the determination of concentrations of alkyl lithium reagents. A sharp color change is observed at equivalence, the solution becoming orange upon initial production of the tosylhydrazone dianion. 1,3-Diphenyl-2-propanone tosylhydrazone is conveniently prepared, stored and handled, and is non-hygroscopic.

Alkyl lithium reagents play a prominent role in organic synthesis and as a consequence the literature abounds with techniques which allow for their accurate determination [1–4]. These procedures, however, are generally lacking in experimental ease, and we therefore sought to develop a method which, in addition to providing results comparable to existing procedures, has as its major strengths both convenience and simplicity. Kofron [5] has reported that diphenylacetic acid in tetrahydrofuran (THF) solvent may be titrated with an alkyl lithium solution to a yellow lithium α -lithiodiphenylacetate endpoint, but this dianion is only weakly colored and endpoint determination is therefore somewhat subjective. We present here an improvement on this procedure which is based on conversion of 1,3-diphenyl-2-propanone tosylhydrazone (I) in THF to the intensely colored dianion (III) (Scheme 1).

The conversion of tosylhydrazones containing α -hydrogen atoms to alkenes by the action of ≥ 2 equivalents of alkyl lithium reagent is well-known [6], and has been demonstrated to proceed via a dianion intermediate [7]. Dianion formation in THF solution is quantitative and nearly instantaneous even at -50°C in systems containing primary or secondary α -hydrogen atoms [8]. Although in our hands all tosylhydrazone dianions give colored solutions in THF, the compound chosen for the present study yields the sharpest endpoint. The end-

SCHEME 1



point is easily observed as a change from the nearly colorless monoanion to orange indicating the presence of the dianion III. The results of our study using a variety of alkyllithium solutions appear in Table 1.

The described technique offers a rapid, simple, and definitive solution to an often encountered problem. The key reagent, 1,3-diphenyl-2-propanone tosylhydrazone, is non-hygroscopic, is conveniently prepared and easily stored without any precautions. Finally, the endpoint is sharp and the values obtained in the titration of alkyllithiums using this tosylhydrazone method agree well with those found using established procedures.

TABLE 1
DETERMINATION OF ALKYL LITHIUM SOLUTIONS

Alkyl lithium Reagent ^a	Tosylhydrazone ^b Determination (Molarity)	Independent Determination (Molarity)
Methyl lithium	1.66 ± 0.08	1.68 ^c ± 0.04
Phenyl lithium	2.01 ± 0.02	2.00 ^d ± 0.11
n-Butyl lithium	1.35 ± 0.02	1.39 ^d ± 0.02
t-Butyl lithium	1.49 ± 0.05	1.51 ^c ± 0.05

^a All alkyl lithium reagents used were from previously opened containers available from commercial suppliers. ^b Values obtained represent the average of triplicate runs. ^c Value obtained represents the average of triplicate runs using the procedure cited in Ref. 3. ^d Value obtained represents the average of triplicate runs using the procedure cited in ref. 2.

Experimental

Materials

All glassware was dried overnight at 140°C prior to use. Reagent grade tetrahydrofuran was purchased from Mallinckrodt and dried by distillation from sodium metal/benzophenone immediately prior to use. Alkyl lithium solutions were purchased from Aldrich Chemical Company. 1,3-Diphenyl-2-propanone was purchased from Eastman Chemical Company. Tosylhydrazine may be purchased from Eastman Chemical Company or prepared by the convenient procedure of Friedman [9].

Instrumentation

Mass spectra were obtained on a Hitachi Perkin Elmer RMU-6 at 70 eV ionizing voltage. PMR spectra were run on a Varian T-60 instrument. Infrared spectra were recorded on a Perkin Elmer 167. Melting points were determined with a Thomas Hoover capillary apparatus and are uncorrected.

1,3-Diphenyl-2-propanone tosylhydrazone

In a 50 ml Erlenmeyer flask, tosylhydrazine (1.86 g, 10 mmol) is dissolved in 30 ml hot ethanol containing a trace of conc. HCl. 1,3-Diphenyl-2-propanone (2.10 g, 10 mmol) is added, the contents of the flask swirled and allowed to cool to room temperature. Cooling to -15°C in a freezer overnight completes crystallization and the product is isolated by suction filtration. Washing with 5 ml cold ethanol followed by drying at ambient temperature in a vacuum dessicator (0.3 torr, 3 h) yields 3.41 g, 91% yield, 1,3-diphenyl-2-propanone tosylhydrazone, m.p. 185–186°C (d). The reagent may be stored in an amber bottle on the shelf and requires no protection from ordinary atmospheric moisture. PMR (CDCl₃, TMS) δ: 2.44(s, 3), 3.38 (s, 2), 3.49 (s, 2), 6.57–7.64 (m, 15), ppm. Mass spectrum; *m/e* (rel. int.): 378 (*M*⁺ 1), 117 (19), 178 (23), 124 (26), 103 (29), 179 (32), 65 (32), 116 (34), 193 (35), 92 (36), 115 (46), 194 (54), 223 (55), 91 (100). IR (film): 3200, 1630, 1600, 1495, 1330, 1165, 1030, 815, 755, 695 cm⁻¹.

Procedure for titrations using 1,3-diphenyl-2-propanone tosylhydrazone

An oven dried 50 ml Erlenmeyer flask containing a magnetic stir bar is charged with an accurately weighed portion (~1.0 mmol) of the tosylhydrazone. The flask is fitted with a rubber serum cap, an inlet for scrubbed nitrogen and a vent and is flushed with the inert gas. Anhydrous THF (10 ml) is then added and stirring continued until the tosylhydrazone dissolves. The flask is cooled to 0°C by means of an ice bath * and the alkyllithium reagent run in dropwise ** via a 1.00 ml syringe (graduated by 0.01 ml) until the orange color indicative of dianion formation persists.

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References

- 1 H. Gilman and F.K. Cartledge, *J. Organometal. Chem.*, 2 (1964) 447.
- 2 R.L. Eppley and J.A. Dixon, *J. Organometal. Chem.*, 8 (1967) 176.
- 3 S.C. Watson and J.F. Eastham, *J. Organometal. Chem.*, 9 (1967) 165.
- 4 H. Gilman and A.H. Haubein, *J. Amer. Chem. Soc.*, 66 (1944) 1515.
- 5 W.G. Kofron and L.M. Baclawski, *J. Org. Chem.*, 41 (1976) 1879.
- 6 For a recent review see R.H. Shapiro, *Org. Reactions*, 23 (1976) 405.
- 7 R.H. Shapiro, M.F. Lipton, K.J. Kolonko, R.L. Buswell and L.A. Capuano, *Tetrahedron Lett.*, (1975) 1811.
- 8 M.F. Lipton and R.H. Shapiro, *J. Org. Chem.*, 43 (1978) 1409.
- 9 L. Friedman, R.L. Little and W.R. Reichle, *Org. Synth.*, 40 (1960) 93.

* The titration is run in the cold to minimize errors associated with the reaction of the alkyllithium with solvent (see ref. 3).

** Rapid addition of the alkyllithium causes a premature coloration of the solution and loss of endpoint sharpness.