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High Frequency Titrimetric Determination of the Electron Deficiency in Lithium Alkyls¹

Sir:

Organometallic reagents, including lithium alkyls, are generally referred to as strong bases because of their "carbanion character" and gross reactions, *i.e.*, proton abstraction or attachment to Lewis acids.² Various authors have, however, conceived of the structure of certain organometallics in terms of a bonding electron deficiency.³ This deficiency could result in character-

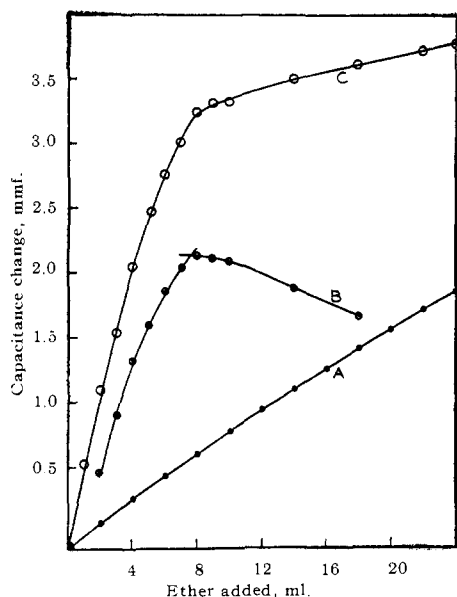


Fig. 1.—Curve A shows the change in capacitance of a cell containing 90 ml. of a hexane solution to which was added increments of ether. Curve C shows same except 0.144 equiv. of butyllithium was present. Curve B is the difference between C and A. Titrations were carried out at 25° (ether = 9.5 M).

istic acidic properties. Specifically, it recently has been suggested that the basic structural unit of a lithium alkyl is a dimer R_2Li_2 ,^{1,4} which associates with itself $(\text{R}_2\text{Li}_2)_n$ as a solid and in nonpolar solvents. If this specific suggestion is correct, by application of the $2(n-1)$ rule of Longuet-Higgins,^{3a} it may be predicted that just two electrons are needed to satisfy the deficiency of each dimer structure. To investigate this

(1) Paper IV in the series "Solvent Effects in Organometallic Reactions." Paper III: Z. K. Cheema, G. W. Gibson, and J. F. Eastham, *J. Am. Chem. Soc.*, **85**, 3517 (1963).

(2) Cf. R. Waack and M. A. Doran, *ibid.*, **85**, 4042 (1963); G. Wittig, *Bull. soc. chim. France*, [5] 1352 (1963).

(3) Cf. (a) H. C. Longuet-Higgins, *Quart. Rev. (London)*, **11**, 121 (1957); (b) G. E. Coates, "Organometallic Compounds," 2nd Ed., Methuen, London, 1960, pp. 44, 57, 131, 152 ff.; (c) M. Weiner and R. West, *J. Am. Chem. Soc.*, **85**, 485 (1963).

(4) V. H. Dietrich, *Acta Cryst.*, **16**, 681 (1963).

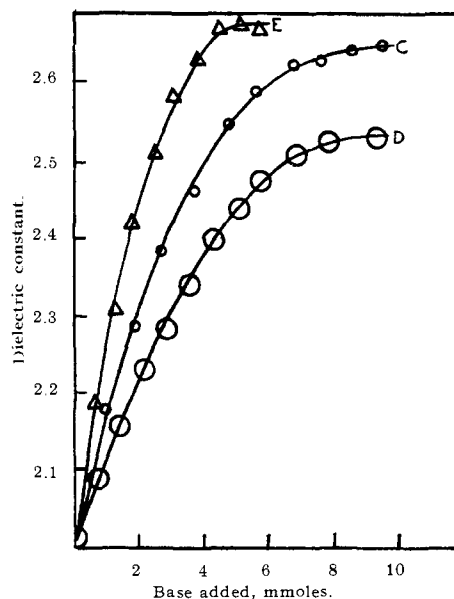
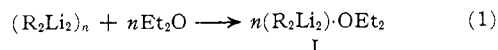


Fig. 2.—Apparent dielectric constants of three hexane solutions, each of 7 ml. volume and containing 11.2 mequiv. of butyllithium, to which Lewis bases were added: D, triethylamine; C, diethyl ether; E, tetrahydrofuran.

prediction experimentally, we have measured the change in dielectric properties of several lithium alkyls consequent to their titration with Lewis bases.

Figure 1 shows the changes in dielectric properties of 90 ml. of hexane solution in a high frequency capacitance cell⁵ to which increments of diethyl ether (Et_2O) were added: curve A for hexane originally alone and curve C for hexane containing 0.144 equiv. of RLi , *n*-butyllithium. Although an RLi solution in hexane is hardly more polar than hexane alone, it is seen that addition of ether causes a relatively steep rise in the dielectric character of the solution (more change in the dielectric than ether alone causes) and that this rise is complete when the ratio of RLi to Et_2O is 2:1. This latter fact is more apparent from a plot B of the difference between curves A and C. In effect, C is a titration curve for a reaction (eq. 1) in which the lithium alkyl is an "acid." There would seem to be some practical potential in titrations of this type, particularly with a differential curve like B, for nondestructive analysis of alkyllithium solutions.



It was conceivable that the Et_2O titration curve did not corroborate the prediction of each R_2Li_2 unit accepting just one pair of electrons to satisfy the organometallic's bonding electron deficiency; Et_2O does have two pairs of nonbonding electrons which it could be contributing in structure I. To check this consideration, high frequency titrations of butyllithium in hexane were carried out with triethylamine (Et_3N) instead of Et_2O as the base. As Fig. 2, curve D, shows, Et_3N also causes a rise in dielectric character, and the steep rise is complete with the addition of one pair of nonbonding electrons from the base for every R_2Li_2 unit in solution. Hydrocarbon solutions of several lithium alkyls (ethyl, *sec*-butyl, *t*-butyl, *n*-butyl), each with several different

(5) A 5-Mc. signal was applied concentrically to the all-glass cell and measured with the circuit of a Sargent Model V oscilloscope modified so that capacitance change was linear with dielectric constant change within the cell and so that the cell could be operated in a controlled atmosphere.

bases (tetrahydrofuran, dioxane, triethylamine, diethyl ether), have been used in analogous experiments with consistent results; some individual points are noteworthy.

The polarity of the R_2Li_2 -base complexes (*cf.* eq. 1) in hexane is not a function of Lewis base strength. To obtain curves D, C, and E in Fig. 2, Et_3N , Et_2O , and THF (tetrahydrofuran), respectively, were added to equal amounts of *n*-butyllithium. It is seen that the least increase in dielectric constant is with Et_3N , the strongest base; that the greatest increase is with THF suggests that steric requirements by the base are important. This suggestion is supported by the facts that with Et_2O *sec*-butyllithium behaves like the *n*-butyl isomer, but with Et_3N the bulkier *sec*-butyl isomer shows considerably less dielectric change. Apparently the still bulkier *t*-butyllithium dimer cannot associate at all with Et_3N ; attempted titration of the *t*-butyl isomer in hexane, where it is known^{3c} to exist as $(R_2Li)_2$, shows no dielectric change with Et_3N . With THF, a base of low steric requirements, *t*-butyllithium is precipitated from hexane.⁶ Even *n*-butyllithium is precipitated from hexane by addition of the "diacidic" base, dioxane.⁷

An interesting question is whether the acidic character of R_2Li_2 which results in eq. 1 should be called Lewis acidity. An ordinary Lewis acid accepts an electron pair with an unoccupied nonbonding atomic orbital (commonly a p-AO); such acidic character is not a consequence of a deficiency of bonding electrons. The electron pair accepted by R_2Li_2 is surely going to fill an unoccupied molecular orbital (probably a π -MO)⁸; such acidic character is one of bonding electron deficiency. It would seem best to describe R_2Li_2 in hexane simply as electrophilic (perhaps akin to description of an organic dienophile as electrophilic) and to say that structure I is a π -complex. The possible utility of these concepts, the electrophilic character of lithium reagents in hydrocarbons and the neutralization of this character with ethers, is apparent in mechanistic consideration of numerous reactions, *e.g.*, polymerization of olefins by lithium alkyls, which can be stereospecific in hydrocarbons (*ergo* "electrophilic" propagation?) but not when ether is present (*ergo* "anionic" propagation?).

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(6) All titrations of the branched-chain lithium reagents must be carried out at low temperature to avoid the known chemical decomposition of the organometallics by ethers; *cf.* ref. 3b, pp. 7-8. To precipitate *t*-butyllithium from hexane with THF, care must be taken to add no more than the 1 equiv. of base per 2 of organometallic, *i.e.*, just enough to give R_2Li_2 :THF, because excess THF redissolves the complex, which then undergoes the exothermic chemical decomposition.

(7) Although the precipitated complex has not yet been satisfactorily analyzed, it is presumably R_2Li_2 :dioxane: R_2Li_2 .

(8) Almost any theoretical (LCAO) analysis of R_2Li_2 will indicate some low level unoccupied bonding MO for the species. Recently we have found additional experimental evidence for such an MO; these species show specific absorption bands in the ultraviolet region characteristic of π -chromophores.

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Volume Changes Accompanying the Adenosine Triphosphate-Myosin B Interaction

Sir:

Hypothesis¹ as well as experiment² suggests that in the interaction between adenosine triphosphate (ATP) and the contractile protein system, myosin B, water molecules are released from a bound state. If so, the interaction may entail a change in the volume of the system. To determine whether this volume change occurs is complicated by the concomitant hydrolysis of ATP to adenosine diphosphate (ADP) and inorganic phosphate (Pi); any volume change accompanying the hydrolysis superimposes upon and obscures the volume change arising from the structural reaction or "superprecipitation."¹ Because the structural effect occurs only early in the reaction, while the hydrolysis effect continues until ATP is exhausted, it is conceivable that the structural effect may be inferred from a suitable extrapolation to time zero.

In the present note we report an attempt to resolve these effects, using conventional Linderstrom-Lang dilatometers³ immersed in an accurately controlled constant temperature bath. Figure 1 shows the time course of the volume change resulting from the addition of 3 ml. of 0.030 *M* ATP to 14 ml. of a 1% suspension of myosin B when both constituents are in 0.06 *M* KCl + 0.04 *M* tris(hydroxymethyl)aminomethane-maleic acid buffer, pH 7.00, at 26°. (Fig. 1 has been corrected for the volume change accompanying dilution

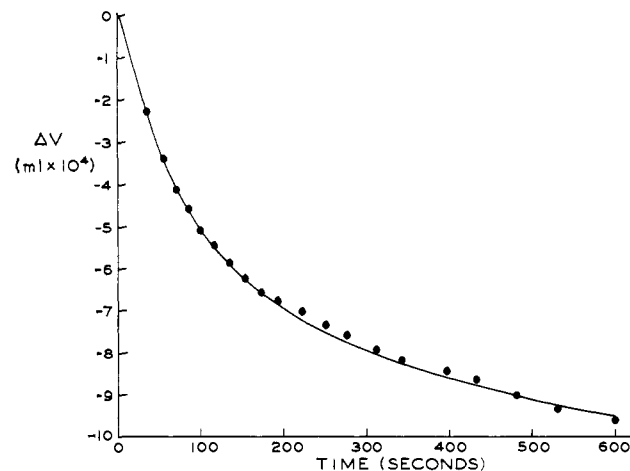


Figure 1.

of ATP; the volume change accompanying dilution of the protein is negligible). Mixing was achieved by magnetic stirring, and the plug due to superprecipitation was clearly formed within the first 2 min. of reaction. When P_i liberation is measured under the same conditions it is found that the ATP is about 95% dephosphorylated in 10 min. If the volume increment is plotted against the $[P_i]$ increment (Fig. 2), the slope of the graph indicates that ΔV_{obsd} is 10.9 ml./mole of ATP split. Since^{4,5}

$$\Delta V_{\text{dephosph}} = \Delta V_{\text{obsd}} + \phi \sum_i R_i \Delta V_i$$

(1) A. Szent-Gyorgyi, "Chemistry of Muscular Contraction," Academic Press, Inc., New York, N. Y., 1947, p. 38.

(2) R. V. Rice, H. Asai, and M. F. Morales, *Proc. Natl. Acad. Sci.*, **50**, 549 (1963).

(3) J. Rasper and W. Kauzmann, *J. Am. Chem. Soc.*, **84**, 1771 (1962).

(4) R. J. Podolsky and M. F. Morales, *J. Biol. Chem.*, **218**, 945 (1956).

(5) S. A. Bernhard, *ibid.*, **218**, 961 (1956).