

polarimetric method because their half-lives are too short to permit easy optical resolution, and probably to some compounds which cannot be resolved optically because they are symmetric even in the absence of rotation.⁶

Further examples as well as other useful stereochemical information derivable from n.m.r. spectra of such diphenyls will be reported in due course.

Acknowledgments.—It is a pleasure to express our gratitude to Professor M. S. Newman for a generous sample of the diester IIB, made by R. B. Meyer while working on an N.S.F. project at The Ohio State University, to Drs. R. Ferreira and T. Ando and Professor H. Shull for helpful discussions concerning the theoretical treatment of the kinetic data, to Mr. A. O. Clouse for assistance with some of the n.m.r. measurements, and to Mr. S. W. Young and the Indiana University Research Computing Center for assistance with the computations. The work was supported in part by a grant to W. L. M. from the Petroleum Research Fund, administered by the American Chemical Society, and one to R. B. M. from the Monmouth College Faculty Research Fund, to whom we express thanks. The n.m.r. instruments were provided by grants from the National Science Foundation and the U. S. Public Health Service, National Institutes of Health, to whom we are grateful.

DEPARTMENT OF CHEMISTRY
INDIANA UNIVERSITY
BLOOMINGTON, INDIANA

WALTER L. MEYER

DEPARTMENT OF CHEMISTRY
MONMOUTH COLLEGE
MONMOUTH, ILLINOIS

ROBERT B. MEYER

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Solvent Effects in Organometallic Reactions. II

Sir:

Although no quantitative data from kinetic evaluations of such solvent effects have been reported previously, it is generally recognized that certain solvent types (particularly ethers) are "good" for organometallic reactions. We wish to report here quantitative findings on the variation in rates of reaction between *n*-butyllithium (BuLi) and 1-bromoöctane (RBr) as a function of the composition of the solvent system hexane-ether. The findings are revealing as to the basis of the virtue of ether as solvent in this reaction and as to structures both of butyllithium itself and of the transition state for this reaction.

Samples from hexane-ether solutions (made up with known initial concentrations of reactants and maintained at 27° in an atmosphere of nitrogen) were quenched with water and analyzed for product and reactant content by gas chromatography. Plots with the appropriately integrated equations, and other standard tests, showed that the data fit the second-order rate law (1)¹ to a fraction of reaction >90% with good reproducibility. A plot of several k_a

$$\text{rate} = k_a(\text{BuLi})_a(\text{RBr})_a \quad (1)$$

values *vs.* the concentration of ether in the mixed solvent is shown in Fig. 1 for the range *ca.* 3–50% ether. The regular increase in k_a with added ether (the positive slope in Fig. 1) is not surprising; it would be an expected consequence of the polar solvent's effect on a reaction involving some increase in charge separation in the transition state. The unexpected feature of the slope in Fig. 1 is that it does not extrapolate back to

(1) The subscripts *a* in eq. 1 indicate that the concentration terms represent apparent total or stoichiometric concentrations.

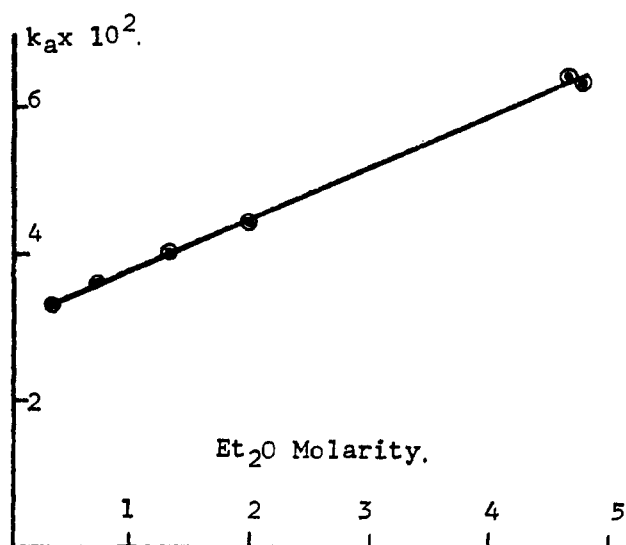
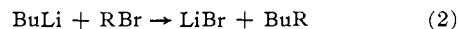


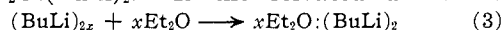
Figure 1.

an intercept even nearly approximating the low rate constant for reaction in pure hexane. The facts are that the rate of formation (2) of dodecane (BuR) is increased by a factor of over 10^3 in going from hexane to ether as solvent,² but that virtually all of this large acceleration is effected when only a very small amount of ether has been added to the hexane reaction solution, *i.e.*, before the first point shown in Fig. 1. In other words, there is an additional, and much larger, solvent effect by ether on this reaction in hexane.



Acceleration of the coupling reaction by low concentrations of ether, (Et₂O), is not a function of this concentration itself, but rather is affected by the ratio, *r*, of ether to butyllithium, (Et₂O)/(BuLi). Figure 2 shows that k_a is a linear function of *r* up to a value of *r* = 0.5,³ after which additional ether effects the relatively small acceleration already indicated in Fig. 1. The linearity of Fig. 2 to *r* = 0.5 and the rather sharp break thereafter strongly suggest a structural significance for this *r*-value. Thus, the virtue of ether as a solvent is primarily a consequence of a highly effective specific solvation phenomenon and only secondarily due to its macroscopic solvent properties, *e.g.*, dielectric constant.

We interpret the low reactivity of butyllithium in hexane to result from a large degree of association or polymerization of the organometallic reagent in the hydrocarbon solvent, and the primary solvent effect of ether to be depolymerization of the reagent. It is our hypothesis that the basic structural unit for an alkyl-lithium is a dimer, (BuLi)₂, which associates in hexane to tetramers, hexamers, etc. ((BuLi)_{2x}); in ether the highly associated form dissociates (3) to the solvated dimer, Et₂O:(BuLi)₂.⁴ If the solvated dimer form



(2) In the hydrocarbon solvent, coupling is sufficiently slow that reduction becomes the major reaction; paper I in this series: J. F. Eastham and G. W. Gibson, *J. Org. Chem.*, **28**, 280 (1963).

(3) In Fig. 2, k_a values are from "initial rates," because at low ether concentrations *r* changes significantly as the reaction proceeds; these values were verified over a fourfold variation in butyllithium concentration (0.33–1.32 *M*).

(4) Our ideas on the geometry of a solvated dimer of butyllithium will be published subsequently; the concept of a four-membered (dimeric) ring involving two three-center bonds is indicated for several other organometallics; *cf.*, G. E. Coates, "Organo-Metallic Compounds," 2nd Ed., Methuen, London, 1960, pp. 57, 99, 131–133, etc. Greater association of alkylolithiums in hydrocarbon solvents has been considered extensively; *cf.*, T. L. Brown, D. W. Dickerhoof and D. A. Bafus, *J. Am. Chem. Soc.*, **84**, 1371 (1962), who propose structures for the tetramers and hexamers of alkylolithiums in a hydrocarbon and specifically consider their disruption by basic solvents.

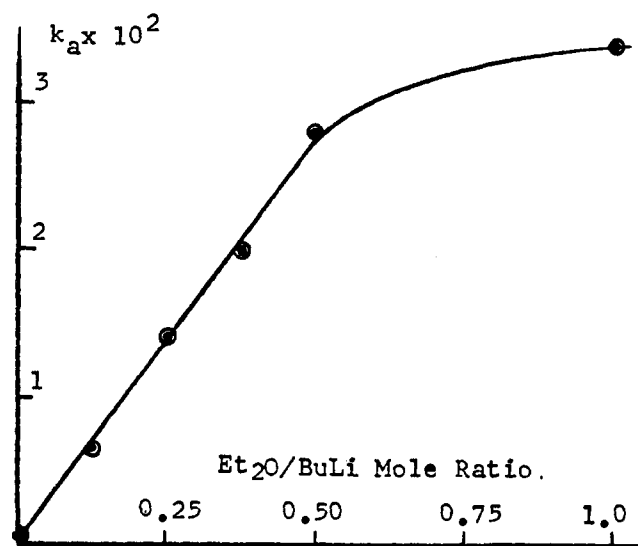
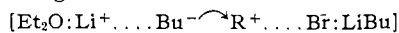


Figure 2

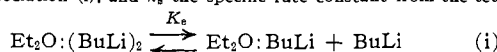
is much more reactive than the highly associated form (or even if the two forms are of the same reactivity but α is large), the kinetically effective concentration of butyllithium (*i.e.*, dimer concentration) will be the fraction $1/2$ ($r/0.5$) of the stoichiometric concentration of butyllithium, and apparent rate constants will be proportional to r , up to and not beyond $r = 0.5$, as in Fig. 2.

From the above interpretation it follows that even though the reaction is first order in the stoichiometric concentration of the organometallic, the transition state for the coupling reaction (2) contains two molecules of butyllithium (and one each of ether and alkyl halide, or tetramolecular over-all). This bimolecularity in organometallic obviously results if the dimer directly attacks alkyl halide in a rate-determining step, and can be shown to result even if the dimer is in an equilibrium with monomers which attack the alkyl halide.⁵ We suggest that the transition state for coupling (2) is attained when the alkyl halide, assisted by butyllithium acting as a Lewis acid, furnishes an incipient alkyl carbonium ion to another molecule of butyllithium, in turn assisted in furnishing a butyl carbanion by ether acting as a Lewis base. The main features (but not the geometry) of this transition state may be roughly represented by the bracketed structure below. While this transition state was conceived on the basis of the reaction being tetramolecular, the proposed structure with its high degree of ionic character in the indicated bonds is also consistent with (a) the general solvent effect (Fig. 1) on the rate of this reaction, (b) the ease of racemization of asymmetric carbon bearing the halogen atom in this reaction⁶ and (c) the effectiveness of ether in racemizing asymmetric carbon bearing a lithium atom.⁷



In the few other reports on rates of organolithium reactions,⁸ the possible influence of association of these

(5) In the latter case if K_e represents a very small equilibrium constant for dimer dissociation (i), and k_s the specific rate constant from the tetra-



molecular rate law (ii), then the apparent rate constant k_a is the product rate = $k_s(\text{Et}_2\text{O}:\text{BuLi})(\text{BuLi})(\text{RBr})_a$ (ii)

$1/2(k_s K_e)$ and data will follow law 1.¹

(6) H. D. Zook and R. N. Goldey, *J. Am. Chem. Soc.*, **75**, 3975 (1953).

(7) R. L. Letsinger, *ibid.*, **72**, 4842 (1950); D. Y. Curtin and W. J. Koehl, *Chem. Ind. (London)*, 262 (1960).

(8) T. F. Fagley and E. Klein, *J. Am. Chem. Soc.*, **77**, 786 (1955); S. J. Cristol, J. W. Ragsdale and J. S. Meek, *ibid.*, **73**, 810 (1951); C. G. Swain and L. Kent, *ibid.*, **72**, 518 (1950).

reagents on the kinetic order of their reactions has not been considered. While the reality of our suggested dimeric structure in ether is by no means assured, it would seem important in any future such kinetic studies at least to consider the possibility that "first order in stoichiometric alkyllithium" indicates a reaction which is actually bimolecular in this reagent.

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DEPARTMENT OF CHEMISTRY
UNIVERSITY OF TENNESSEE
KNOXVILLE, TENNESSEE

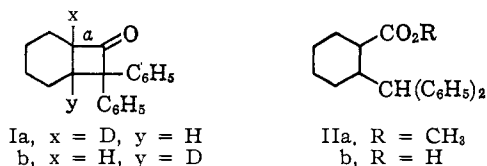
JEROME F. EASTHAM
GERALD W. GIBSON

RECEIVED MARCH 27, 1963

Hydrogen Isotope Effects and the Mechanism of Cycloaddition

Sir:

Whether in cycloaddition reactions the new bonds form simultaneously is a current problem¹ that might be solved by studying the effects of isotopic substituent changes, for of all substituent effects, the theoretical interpretation of this one would be expected to be most meaningful. The reaction² of diphenylketene with 1-deuteriocyclohexene was examined, therefore, to see whether the two products, Ia and Ib, were formed in significantly different amounts.



Equimolar quantities of the reactants, cyclohexene-1d³ and diphenylketene, combined with a trace of hydroquinone in a sealed tube, were heated at 100° for 10 days. The adduct, m.p. 131.5–132.5°, isolated by recrystallization from *n*-hexane, was analyzed for its total deuterium content and the fraction of the deuterium atoms attached to the carbon adjacent to the carbonyl then was determined by washing out these atoms with protonic solvents, recrystallizing from 95% ethanol and analyzing the resultant product for the remaining deuterium. Three different procedures were used to wash out the enolizable deuteriums (Table I). (1) The adduct was refluxed with methanolic sodium methoxide, re-isolated and analyzed. (2) The ester IIa, a major side-product in this procedure, was isolated and the corresponding acid^{2,4} IIb, m.p. 154–156°, obtained by its saponification, was analyzed. (3) Lastly, the adduct was treated at 80° with a dilute solution of hydrochloric acid in acetic acid, from which it could be re-isolated in quantitative yield, and the washing was repeated until the analysis was constant.^{5–8}

(1) (a) R. B. Woodward and T. J. Katz, *Tetrahedron*, **5**, 70 (1959); (b) J. D. Roberts and C. M. Sharts, "Organic Reactions," Vol. 12, John Wiley and Sons, Inc., New York, N. Y., 1962, pp. 1–56.

(2) (a) H. Staudinger and E. Suter, *Chem. Ber.*, **53**, 1092 (1920); (b) E. H. Farmer and M. O. Farooq, *Chem. Ind. (London)*, **56**, 1079 (1937); *J. Chem. Soc.*, 1925 (1938); (c) L. I. Smith, C. L. Agre, R. M. Leekley and W. W. Pritchard, *J. Am. Chem. Soc.*, **61**, 7 (1939).

(3) Prepared from D₂O and 1-lithiocyclohexene (made by treatment of 1-chlorocyclohexene in ether with Li containing 0.8% Na). The ratio of non-olefinic to olefinic protons as determined from its n.m.r. spectrum was 7.62 ± 0.08. The mass spectrum indicated that the sample contained 1.4% C₆H₁₀, 97.9% C₆H₉D and 0.7% C₆H₈D₂. We are indebted to Dr. Eric O. Forster, Esso Research and Engineering Co., for his good offices in obtaining this analysis.

(4) This is probably the *trans* isomer.