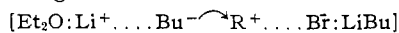


Figure 2

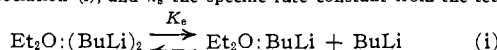
is much more reactive than the highly associated form (or even if the two forms are of the same reactivity but α is large), the kinetically effective concentration of butyllithium (*i.e.*, dimer concentration) will be the fraction $1/2$ ($r/0.5$) of the stoichiometric concentration of butyllithium, and 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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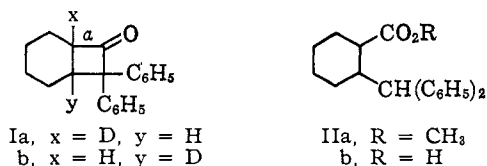
JEROME F. EASTHAM
GERALD W. GIBSON

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-1-*d*³ 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.

TABLE I

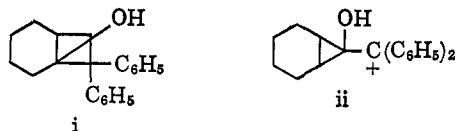
Sample No.	Compound and its origin	Deuterium analysis (atom % excess D) ^a	k_{1a}/k_{1b} ^b
1	I, original adduct	4.67, 4.69, 4.73, 4.70	
2	I, 1 after 19-hr. base wash ^c	2.23	1.11
3	IIb ^d	2.01, 2.03	1.11
4	I, original adduct	4.63, 4.64, 4.65	
5	I, 4 after 18-hr. base wash	2.24, 2.24	
6	I, 5 after 14.5-hr. base wash	2.21, 2.15, 2.16, 2.17	1.14
7	IIb ^d	2.02	1.09
8	I, original adduct	4.71, 4.70, 4.72	
9	I, 8 after 3-hr. acid wash ^e	2.55, 2.56	
10	I, 9 after 3-hr. acid wash	2.30	
11	I, 10 after 3-hr. acid wash	2.23, 2.24	
12	I, 11 after 6-hr. acid wash	2.15	
13	I, 12 after 6-hr. acid wash	2.16, 2.17	1.18
Average isotope effect			1.13 ± 0.03

^a Analyses by the falling drop method were performed by Josef Nemeth, Urbana, Illinois. ^b The ratio of the two products Ia and Ib. The probable error in this ratio is ±0.03. ^c A solution of I (0.07 M) and NaOCH₃ (0.2 M) was refluxed in CH₃OH. ^d From saponification of the IIa isolated in the preparation of the preceding sample of I. ^e I was heated at 80° in a large excess of a mixture of 10 parts of glacial acetic acid and 1 part of a solution of 10% HCl (1 volume of concentrated HCl and 3 volumes of water).

The observed excess of Ia indicates that, at the transition state determining the formation of the product, bond formation is not symmetrical (*i.e.*, the bonds are not equally formed). The magnitude of the isotope effect (1.13 ± 0.03) is similar to the maximum secondary α -deuterium effect observed in numerous solvolytic,⁹ thermal cleavage¹⁰ and addition¹¹ reactions, in which the isotope effect has been attributed to mass-sensitive changes in vibrational frequencies¹² or steric crowding¹³ accompanying rehybridization of the carbon bearing hydrogen. If the bond *a* in I were formed first, deuterium would be expected to accumulate on the carbon atom adjacent to the carbonyl. The observation of this effect indicates that the transition state is asymmetrical in this sense. The opposite should be expected if the inductive effect of deuterium or the β -isotope effect were dominant.^{14,15}

The technique described in this communication is applicable only to cycloaddition reactions between one

(5) Heating I and a 3:1 mixture of acetic acid and 10% HCl on a steam bath removed not only the deuterium atoms on the carbon adjacent to the carbonyl, but some of the remaining deuteriums as well, which might indicate that homoionization to (i) occurs,⁶ but more probably represents a cyclo-butyl-cyclopropylcarbonyl rearrangement⁷ to (ii) and its reversal.



- (6) A. Nickon and J. L. Lambert, *J. Am. Chem. Soc.*, **84**, 4604 (1962).
 (7) M. S. Silver, M. C. Caserio, H. E. Rice and J. D. Roberts, *ibid.*, **83**, 3671 (1961), and earlier papers.
 (8) The reaction was not appreciably reversible. Simultaneously with one of the addition reactions, adduct I (sample 4) was heated with a 16 M excess of cyclohexene, after which it contained 4.56 atom % of excess D.
 (9) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962; see also R. Stewart, A. L. Gatzke, M. Mocek and K. Yates, *Chem. Ind. (London)*, 331 (1959).
 (10) S. Seltzer, *J. Am. Chem. Soc.*, **85**, 14 (1963); **83**, 2625 (1961).
 (11) (a) S. Seltzer, *ibid.*, **83**, 1861 (1961); (b) D. B. Denney and N. Tunnel, *Chem. Ind. (London)*, 1383 (1959); (c) M. Feld, A. P. Stefani and M. Szwarc, *J. Am. Chem. Soc.*, **84**, 4451 (1962); (d) M. Takahashi and R. J. Cvetanovic, *Can. J. Chem.*, **40**, 1037 (1962); (e) G. A. Olah, S. J. Kuhn and S. H. Flood, *J. Am. Chem. Soc.*, **84**, 1688 (1962); (f) D. E. van Sickle, *Tetrahedron Letters*, 687 (1961); (g) S. Seltzer, *ibid.*, 457 (1962).
 (12) A. Streitwieser, Jr., R. H. Jagow, R. C. Fahey and S. Suzuki, *J. Am. Chem. Soc.*, **80**, 2326 (1958).
 (13) L. S. Bartell, *ibid.*, **83**, 3567 (1961).
 (14) Reviewed by R. E. Weston, Jr., *Ann. Rev. Nucl. Sci.*, **11**, 439 (1961).
 (15) The β -isotope effect might have affected analysis methods 1 and 2 if the ring cleavage were fast compared to enolization, and a lower apparent effect in analysis 1 and a higher one in analysis 2 probably would have resulted [cf. J. M. Jones and M. L. Bender, *J. Am. Chem. Soc.*, **82**, 6322 (1960); M. L. Bender and M. S. Feng, *ibid.*, **82**, 6318 (1960)]. This was not observed.

reactant, symmetrical except in the isotopic substituent, and another so unsymmetrical that if it were to add asymmetrically, it would do so in only one sense.¹⁶⁻¹⁸

Acknowledgments.—We gratefully acknowledge the support of the National Science Foundation (NSF G-15561, GP-748), the Socony Mobil Oil Co. and the Alfred P. Sloan Foundation.

(16) That bond *a* forms first in diphenylketene cycloadditions follows from the isomer specificity observed in its additions to cyclohexadiene, cyclopentadiene, styrene, etc.,¹⁷ as well as from the probable bond dissociation energies¹⁸ of atoms attached to the carbonyl and to the benzhydryl carbon adjacent to the carbonyl.

- (17) Reference 2 and references in ref. 1b.
 (18) C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 50.
 (19) NSF Fellow, 1960-1961; NSF Cooperative Fellow, 1962-1963.

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RECEIVED APRIL 30, 1963

Unusual Nuclear Magnetic Resonance Dilution Shift for Acetic Acid in Acetic Anhydride¹

Sir:

N.m.r. studies of carboxylic acids in electron-donating solvents have revealed a marked concentration-dependence of the chemical shift of the acidic hydrogen.^{2,3} This "dilution shift" is believed to result from a rapid equilibrium between dimeric acid molecules and a monomeric species, probably hydrogen-bonded to a solvent molecule. A difficulty with this interpretation is that the data appear to imply that at moderate concentrations (10 to 20 mole %) considerably more than half of the solute is dimerized. This conflicts with the earlier view⁴ that in such solvents "carboxylic acids associate with the solvent molecules rather than with their own species. Thus they give normal molecular weights in ethers, esters, and ketones." Another alarming symptom is the poor quantitative agreement between two independently determined curves of chemical shift *vs.* concentration for acetic acid (AcOH) in acetone.^{2,3}

If AcOH is dissolved in acetone contaminated with water, rapid proton exchange between water and acid should occur and the observed hydroxyl chemical shift should be the weighted average of the true value for the

- (1) Supported by research grant NSF G-17421 from the National Science Foundation.
 (2) C. M. Huggins, G. C. Pimentel and J. N. Shoolery, *J. Phys. Chem.*, **60**, 1311 (1956).
 (3) L. W. Reeves, *Trans. Faraday Soc.*, **55**, 1684 (1959).
 (4) G. Allen and E. F. Caldin, *Quart. Rev. (London)*, **7**, 278 (1953).