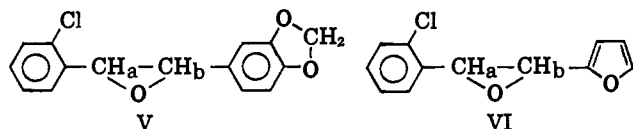


The stereochemistry of IV is preferentially *trans*. A high *trans/cis* ratio is favored by bulky *ortho* and *meta* substituents (*cf.* 2,6-dichlorobenzaldehyde), by moderate reaction conditions and by moderately reactive (hence more selective) reaction partners (*cf.* *p*-chlorobenzaldehyde).

The proposed mechanism is supported and the scope of the reaction is considerably extended also by the synthesis of mixed epoxides. The addition of I, a powerful nucleophile, to a mixture of aldehydes, in which the less reactive aldehyde predominates, yields, in addition to the symmetrical epoxide derived from the more reactive aldehyde, also varying proportions of the mixed epoxides. For instance, the addition of Ia to a mixture of *o*-chlorobenzaldehyde and piperonal (excess) yielded V (*trans*, δ_{Ha} 4.06, δ_{Hb} 3.56, p.p.m., $J = 1.9$ c.p.s.). Similarly, *o*-chlorobenzaldehyde and 2-furaldehyde yielded VI (δ_{Ha} 4.48, δ_{Hb} 3.73 p.p.m. $J = 2.18$ c.p.s.).



The often high yields and the simple, one step, preparative procedure render the present reaction of some interest in synthetic organic chemistry. The mild reaction conditions allow the preparation of epoxides with sensitive structural features, for which some of the most generally used epoxide syntheses (*e.g.*, *via* the olefins by peroxides) are not applicable. For instance, 2-thiophenecarboxaldehyde and Ib ($R = \text{ethyl}$) yielded IV ($R = 2\text{-thenyl}$: δ_{H} (oxirane) *trans* 4.24, *cis* 4.44 p.p.m.; ratio *trans/cis* 1.1). Similarly, 2-pyridinecarboxaldehyde and Ia gave a 90% yield of a reaction mixture, IV ($R = 2\text{-pyridyl}$), which comprised 75% of the *trans* epoxide [m.p. 95–97°; δ_{H} (oxirane) 4.51] and 25% of the *cis* epoxide [δ_{H} (oxirane) 4.73 p.p.m.].

(9) Monsanto Chemicals Corporation, P. O. Box 4388, Philadelphia 18, Pa.

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RECEIVED FEBRUARY 21, 1963

Deuterium Isotope Effect in Intramolecular Insertion Sir:

We here report the first example of isotopic discrimination in liquid phase CH insertion,¹ a reaction presumed to be characteristic of carbene intermediates² and heretofore characterized by unprecedented insensitivity to CH bond strengths.^{2a} We also note that only isotopic discrimination excludes the possibility of ground-state conformational control,³ notorious in intramolecular reactions of low ΔF^\ddagger .

Addition of precooled methylene chloride in tetrahydrofuran to 1,1-di(methyl-*d*₃)ethyl lithium (I) in the same solvent, at -65° , produced deuterated 1,1-dimethylcyclopropane, separated from other products by distillation and gas chromatography.⁴ Analysis by

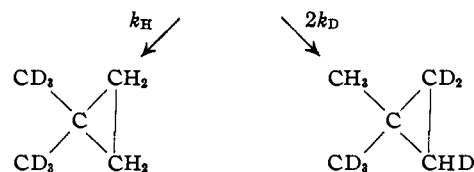
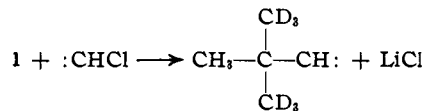
(1) Since the submission of our first draft, J. W. Simons and B. S. Rabino-vitch, *J. Am. Chem. Soc.*, **85**, 1023 (1963), have described deuterium isotope effects of 1.96 and 1.55 for *intermolecular* insertion of ketene-generated CH_2 into allylic and vinylic CH bonds, determined in the gas phase by *intermolecular* competition.

(2) (a) Reviewed by W. Kirmse, *Angew. Chem.*, **73**, 161 (1961); (b) H. E. Simmons and R. D. Smith, *J. Am. Chem. Soc.*, **81**, 4256 (1959); (c) G. L. Closs and J. J. Coyle, *ibid.*, **84**, 4350 (1962).

(3) *Cf.* J. H. Ridd, *Quart. Rev. (London)*, **15**, 418 (1961); A. Streitwieser, Jr., *J. Org. Chem.*, **22**, 861 (1957).

(4) *Cf.* G. L. Closs, Abstracts of papers presented at the 138th National Meeting of the American Chemical Society, September, 1960, p. 9P; *J. Am.*

n.m.r.: (a) excluded the presence of $>3\%$ 1,1-di-methylethyl-*d*₅ chloride in the alkyl lithium precursor; (b) excluded the presence of $>0.8\%$ isomeric alkenes in the purified product; and (c) established the magnitude of the isotope effect. The area ratio, $(\text{CH}_2 + \text{CH})/\text{CH}_3 = 1.47 \pm 0.04$,⁵ unchanged by resubmission of isolated products to reaction conditions, requires that $k_{\text{H}}/k_{\text{D}} = 1.71 \pm 0.06$.



Although similar in magnitude to the low "primary" isotope effects often noted in intramolecular⁶ (and intermolecular) hydride transfer, this result suffers from none of the ambiguities necessarily associated with similar interpretations in the latter reactions.^{6a} Since we have employed intramolecular competition we need not obtain independent kinetic evidence relating the hydrogen migration and rate-determining steps.^{6b,d,7} Since the solvent can play no significant role in the insertion step, no new hydrogen mass-dependent vibrational modes may be acquired by the transition state. The introduction of such modes has been considered the most general source of low $k_{\text{H}}/k_{\text{D}}$ values.⁸

With an unusually meaningful experimental value in hand, we are pleased to discover that it may be derived by the use of only two assumptions, introduced solely for purposes of simplification, but following logically from mechanistic preconception.



(1) Since the reaction is unusually exothermic,⁹ we first assume that the necessarily identical dimensions of the isotopically isomeric transition states, H and D, differ insignificantly from that of their common precursor.¹⁰ The product rule then requires that $3\pi^0 \nu_{\text{H}}^{\text{H}}/\nu_{\text{H}}^{\text{D}} = 1$ and since H and D must at least differ in their unbound frequencies, ν_{L}

$$\frac{k_{\text{H}}}{k_{\text{D}}} = \frac{\sinh h\nu^{\text{D}}/2kT}{\sinh h\nu^{\text{H}}/2kT}$$

where ν^{D} is that frequency in D corresponding to $\nu_{\text{L}}^{\text{H}}$ and ν^{H} is that in H corresponding to $\nu_{\text{L}}^{\text{D}}$.

Chem. Soc., **84**, 809 (1962), W. Kirmse and W. von E. Doering, *Tetrahedron*, **11**, 266 (1960). The mechanism outlined is that proposed by these authors.

(5) Mean and standard deviation of results from three independent experiments using a Varian A-60 instrument.

(6) (a) E. S. Lewis and M. C. R. Symons, *Quart. Rev. (London)*, **12**, 230 (1958), and previous examples cited; (b) S. Winstein and J. Takahashi, *Tetrahedron*, **2**, 316 (1958); (c) C. J. Collins, W. T. Rainey, W. B. Smith and I. A. Kaye, *J. Am. Chem. Soc.*, **81**, 460 (1959); (d) W. B. Smith, R. E. Bowman and J. J. Kmet, *ibid.*, **81**, 997 (1959); (e) D. J. Cram and J. Tadanier, *ibid.*, **81**, 2737 (1959).

(7) L. Melander, "Isotope Effects on Reaction Rates," Ronald Press Co., New York, N. Y., 1960, pp. 103–105, discusses the relative merits of *inter vs. intramolecular* competition in isotope effect determinations.

(8) (a) F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961); (b) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, pp. 190–193; (c) *ref.* 6, pp. 24–32.

(9) We estimate $-\Delta H^\circ = 58 \pm 3$ kcal./mole for "cold" ethyl carbene \rightarrow cyclopropane.

(10) G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955).

(2) We next identify ν_L as a methyl "rocking" mode¹¹ the only characteristic vibration capable of beginning the indicated motion, and choose $-\nu_L^H = \nu^D = 925 \text{ cm.}^{-1}$ and $-\nu_L^D = \nu^H = 765 \text{ cm.}^{-1}$, using neopentane for a model.¹² Since the effective mass approximates that of a methyl group^{11a} tunneling may be neglected. The calculated k_H/k_D , 1.74, may be compared with the observed value of 1.71 ± 0.06 .

In view of this excellent agreement, it should be noted that the simple model specifies the energy, but not necessarily the structure, of the cyclopropane's immediate precursor. In particular, it does not exclude α -lithium neopentyl chloride from this role nor are we aware of any evidence which does. It is hoped that related studies, now in progress, may shed more light on this matter.

(11) (a) W. T. King and B. Crawford, Jr., *J. Mol. Spectry.*, **5**, 421 (1960); **8**, 58 (1962); (b) J. H. Schachtschneider and R. G. Snyder, *Spectrochim. Acta*, **19**, 117 (1963), and references cited therein.

(12) K. Simizu and H. Murata, *Bull. Chem. Soc. Japan*, **30**, 487 (1957).

(13) Taken from the M.S. dissertation of S. J. B., Cornell University, 1963. Partial support, provided by a Frederick Gardner Cottrell grant from Research Corporation, is acknowledged with gratitude.

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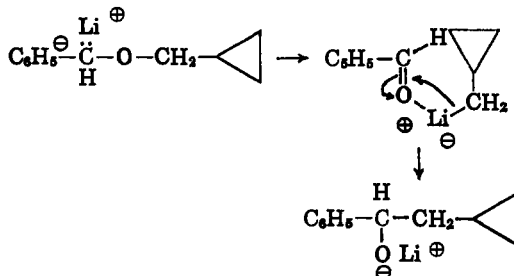
M. J. GOLDSTEIN
S. J. BAUM¹³

RECEIVED APRIL 16, 1963

Cyclopropylcarbinylithium

Sir:

Attempts to prepare the Grignard reagent from cyclopropylcarbinyl bromide and magnesium in the conventional manner have always resulted in the formation of products derivable from allylcarbinylmagnesium bromide.¹ Furthermore, the freshly prepared Grignard reagent itself has been shown to have the allylcarbinyl structure ($\geq 99\%$) by n.m.r. spectroscopy.² We recently have carried out the Wittig rearrangement of cyclopropylcarbinyl benzyl ether and obtained the isomeric carbinol in which the cyclopropylcarbinyl group was largely unrearranged.³ Although the above



pathway, involving an intermediate aldehyde-organolithium complex, seems to be reasonably established,³ it was considered highly desirable to attempt to generate the cyclopropylcarbinyl anion by an independent and unambiguous route, in order to determine its stability with respect to the allylcarbinyl anion. We now wish to report the first preparation of cyclopropylcarbinylithium, using the low temperature metal-halogen exchange reaction⁴ in diethyl ether, a solvent in which the carbon-lithium bond has appreciable ionic character.⁵ This mode of generating carbanions avoids the possible complication of free radical intermediates, as may be the case in forming Grignard reagents.⁶

(1) J. D. Roberts and R. H. Mazur, *J. Am. Chem. Soc.*, **73**, 2509 (1951).

(2) M. S. Silver, P. R. Shafer, J. E. Nordlander, C. Ruchardt and J. D. Roberts, *ibid.*, **82**, 2646 (1960).

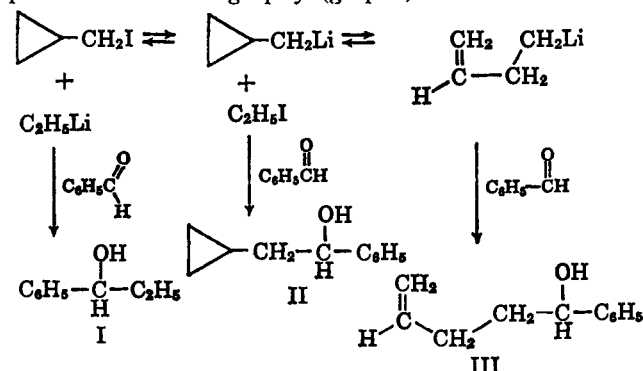
(3) P. T. Lansbury and V. A. Pattison, *ibid.*, **84**, 4295 (1962).

(4) Cf. (a) R. L. Letsinger, *ibid.*, **72**, 4842 (1950); (b) D. E. Applequist and D. F. O'Brien, *ibid.*, **85**, 743 (1963).

(5) D. Y. Curtin and W. J. Koehl, Jr., *ibid.*, **84**, 1967 (1962).

(6) H. M. Walborsky, *Rec. Chem. Progr.*, **23**, 75 (1962).

The generation of cyclopropylcarbinylithium involved the exchange reaction of ethyllithium and cyclopropylcarbinyl iodide in ether at -70° ; the reaction mixture was quenched by reaction with excess benzaldehyde at -70° to yield the corresponding phenylcarbinols which are known⁸ and separable by gas-liquid partition chromatography (g.l.p.c.).



The results of several experiments are summarized in Table I.

TABLE I

No.	mmoles		T, °C.	Exchange time, min.	%		
	C ₂ H ₅ Li	C ₃ H ₇ I			I	II	III
1	1.0	1.0	-70	5	35	49	16
2	1.0	1.0	-70	30	11	51	38
3	1.0	1.0	-70	120	3	17	80
4	10.0	10.0	-70	5	54	18	10
5	10.0	10.0	-18	15	14	0	57

Cyclopropylcarbinyl iodide was prepared from cyclopropylcarbinyl chloride⁷ by bimolecular displacement with sodium iodide in dry acetone. The iodide had b.p. $88-90^\circ$ (150 mm.) and analyzed correctly (Calcd. for C₄H₇I: C, 26.39; H, 3.88. Found: C, 26.56; H, 3.72); its n.m.r. spectrum⁸ showed a broad multiplet at 0.2-1.5 p.p.m. (cyclopropyl protons⁷) and a sharp doublet ($J \sim 8$ c.p.s.) at 3.15 p.p.m. ($-\text{CH}_2-\text{I}$). Less than 1% of cyclobutyl and allylcarbinyl iodides were present, as shown by the extremely weak signals at 4.5, 2.1 and 2.65 p.p.m. (due to cyclobutyl iodide^{4b}) and at 5.2 p.p.m. (due to vinyl protons, even at high spectrum amplitude. In a typical experiment, such as entry 1, the iodide and benzaldehyde (2 mmoles) were placed in separate ampoules, each attached to a separate rod for breaking it, and suspended through a rubber serum cap into the ethyllithium solution (ca. 5 ml.) contained in a test tube. The entire assembly was cooled in a Dry Ice-acetone bath for 30 min. and the ampoule containing the iodide then was broken by pressing the rod through the serum cap. After the appropriate exchange time, the benzaldehyde was introduced similarly and the reaction mixture kept at -70° for 30 min. more, then hydrolyzed and worked up in the usual manner.³ The product mixtures were analyzed by g.l.p.c., on a 5-ft. 30% "Tide" on Chromosorb P column at 135° , using synthetic mixtures of authentic samples⁸ for calibration. Products isolated from preparative g.l.p.c. were checked with standards by infrared spectroscopy. The carbinol yields reported in runs 1-3 are normalized to 100% but in larger scale runs (4 and 5) the actual yield of the three carbinols was 70-80% of theory.⁹

(7) M. C. Caserio, W. H. Graham and J. D. Roberts, *Tetrahedron*, **11**, 171 (1960).

(8) Recorded on a Varian A-60 spectrometer with tetramethylsilane as internal standard and carbon tetrachloride solvent.

(9) In some of the runs small amounts (less than 10%) of benzyl alcohol also were found; this undoubtedly arises from some reduction of benzaldehyde by the organolithium reagents. In most cases, however, benzyl alcohol was not present in greater than trace quantities.