chloride in 8 ml of alcohol-free chloroform for 1 hr. The chloroform layer was separated, and the aqueous layer was extracted with four 3-ml portions of chloroform. The combined extracts were dried over sodium sulfate and concentrated *in vacuo*. The remaining crystalline benzamide was washed several times with pentane to remove traces of benzoyl chloride and then with a small volume of ether, yield 93 mg (76%) of benzamide labeled with ^{15}N, mp 128–129°.

In the mass spectrum the ratio of the intensities of the peaks at *m/e* 122 $(M + 1)^+$ and 121 $(M)^+$ was 0.644 at 70 ev (averaged over three scannings) and 0.622 at 13 ev (averaged over five scannings). From this ratio the abundance of ^{15}N was calculated[35,36] to be 36.2% (from the spectrum at 70 ev) and 36.9% (from the spectrum at 13 ev).

Reaction of I in Acetonitrile-^{15}N. To the labeled acetonitrile (3.2 g) was added 292 mg (2.00 mmoles) of I, 268 mg (1.20 mmoles) of anhydrous magnesium perchlorate, and a little magnesium tosylate. To the stirred reaction mixture was added 355 mg (2.06 mmoles) of anhydrous *p*-toluenesulfonic acid dissolved in 0.5 ml of methylene chloride, by means of a syringe, in 10 min at −30°. The gelatinous mixture was left overnight in a refrigerator. After addition of 5 ml of methylene chloride the precipitate was centrifuged and washed with 2 ml of methylene chloride. The solution was concentrated by distillation *in vacuo*, yielding a solid residue. From the distillate the acetonitrile was recovered by fractional distillation. The precipitate was extracted once with 10 ml of 1,2-dimethoxyethane. This extract was combined with the solid residue and concentrated *in vacuo* leaving the crude product, which was recrystallized from 1,2-dimethoxyethane–methylene chloride (1:5 and ether, yield 327 mg (55%) of the labeled product VI.

Hydrolysis of the Labeled Product VI. A solution of 312 mg of the labeled product VI in 10 ml of water was refluxed for 2.5 hr. Water was removed at reduced pressure leaving an oily residue, which was treated with methylene chloride. Ammonium perchlorate (108 mg, 92%) was collected by filtration. After removal of the solvent, the methylene chloride extract yielded an oil which gave upon sublimation 138 mg (66%) of α-acetaminoisobutyrophenone (VII′). The ratio of peak heights at *m/e* 206 and 205 in the mass spectrum of *unlabeled* VII was 0.674 at 70 ev and 0.445 at 15 ev, for the peaks at 101 and 100 $(C_5H_{10}NO)^+$ the ratio was 0.057 (70 ev), and for the peaks at 59 and 58 $(C_2H_4NO)^+$ it was 0.0358. As calculated[35,36] from the natural abundances of C, H, N, and O, the ratio should read: 0.1367, 0.0598, and 0.0265. The product VII′ obtained from labeled VI showed the following ratio of peak heights: M^+ (206/205), 0.703 at 70 ev and 0.674 at 15 ev; fragment $C_5H_{10}NO^+$ (101/100), 0.595 (70 ev); and fragment $C_2H_4NO^+$ (59/58), 0.566 (70 ev). From the ratios found for the two fragments the abundance of ^{15}N was calculated to amount to 35.0% (fragment $C_5H_{10}NO)^+$ and 35.3% (fragment $C_2H_4NO)^+$. The ammonium perchlorate obtained from the hydrolysis was converted into benzamide by means of the Schotten–Baumann reaction described above, in a yield of 80%. The mass spectrum of this sample of benzamide showed for *m/e* 122 $[(M + 1)^+]$ and 121 (M^+) a ratio of peak heights of 0.092 at 70 ev and 0.096 at 12.5 ev. The mass spectrum of unlabeled benzamide prepared from ammonium perchlorate by the Schotten–Baumann reaction showed for $(M + 1)^+/M^+$ 0.090 at 70 ev and 0.087 at 12.5 ev. As calculated from the natural abundances this ratio should read 0.08097.[36]

Reaction of I with Pyridinium Perchlorate. **a.** To a solution of 1.55 g (8.65 mmoles) of pyridinium perchlorate in 15 ml of pure pyridine was added 1.25 g (8.62 mmoles) of I in 5 min at 0°. The mixture was left in the refrigerator for 14 days. Ether was added and white crystals separated, mp 130–132°, yield 2.65 g (95%). The 3,3-dimethyl-2-phenyl-2-N′-pyridinium aziridine perchlorate (XV) was recrystallized from acetone–ether, mp 131–132°; $\nu_{\max}^{\text{Nujol}}$ 3270 and 1625 cm^{-1}; nmr τ values (acetone-d_6): 8.87 (singlet, 3 H), 8.55 (singlet, 3 H), 6.51 (singlet, 1 H), 2.7–0.3 (multiplet of nine aromatic protons).

Anal. Calcd for $C_{15}H_{17}ClN_2O_4$: C, 55.47; H, 5.27; N, 8.63. Found: C, 55.99; H, 5.43; N, 8.45.

b. To a solution of 364 mg (2.02 mmoles) of pyridinium perchlorate in 4 ml of acetonitrile was added 291 mg (1.00 mmole) of I dissolved in 2 ml of acetonitrile during 5 min at 0°. The mixture was left in the refrigerator for 4 days. The slightly yellow reaction mixture was concentrated *in vacuo* to half-volume, and ether was added. 3,3-Dimethyl-2-phenyl-2-N′-pyridinium aziridine perchlorate was obtained, yield 524 mg (81%). Upon refluxing of the product in acetonitrile solution for 24 hr, pyridinium perchlorate was formed in 89% yield.

c. No reaction occurred with I and trimethylamine perchlorate in acetonitrile solution at room temperature during 2 months.

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(35) The formula for the abundance of $(M + 1)^+$ was employed; the values are not corrected for the natural abundance of ^{15}N.

(36) J. H. Beynon, "Mass Spectrometry and its Applications to Organic Chemistry," Elsevier Publishing Co., Amsterdam, 1960.

Addition of Isopropyllithium in Diethyl Ether to α-Substituted Styrenes. Quantitative Evidence on the Stability of Cyclopropylcarbinyllithium Species

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Contribution from the Department of Chemistry, University of Kansas, Lawrence, Kansas 66044. *Received March 22, 1967*

Abstract: The relative rates of addition of isopropyllithium in diethyl ether at −45° to a series of α-substituted styrenes in which the substituent was ethyl (**1a**), isopropyl (**1b**), 3-pentyl (**1c**), cyclopropyl (**1d**), and *trans*-2-*cis*-3-dimethylcyclopropyl (**1e**) were 28.0, 1.0, 0.6, 310, and 115, respectively. The product of addition of isopropyllithium to **1d** after hydrolysis was 4-phenyl-2-methyl-*cis*-4-heptene (**6**) while addition to **1e** followed by hydrolysis produced a mixture of olefin **8** and cyclopropanes **9, 10,** and **11**. It is concluded that the cyclopropylcarbinyl anion must be stabilized at least in part by conjugative interaction with the cyclopropane ring.

Until now no quantitative evidence has been reported which would allow anything better than a crude comparison of the cyclopropylcarbinyl anion stability with that of structurally related species.

The successful preparation by Lansbury and coworkers[2] of a relatively stable cyclopropylcarbinyl-

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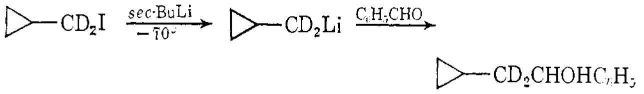
(1) National Science Foundation Cooperative Fellow, 1964–1965. Taken from the Ph.D. Dissertation of J. D. S., University of Kansas, 1966. Partial support from the National Science Foundation and for a special equipment grant from Socony Mobil is hereby acknowledged.

(2) (a) P. T. Lansbury, V. A. Pattison, W. A. Clement, and J. D. Sidler, *J. Am. Chem. Soc.*, **86**, 2247 (1964); (b) P. T. Lansbury and V. A. Pattison, *ibid.*, **85**, 1886 (1963).

lithium-α,α-d_2, in which the deuterium atoms did not scramble, provided confirmation of the previously published molecular orbital calculations of Howden and Roberts[3] which suggested that the bicyclobutonium

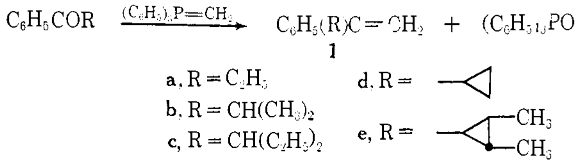


structure would not be the most favored structure for the anion. However, both these calculations and those of Piccolini and Winstein[4] do predict some homoallylic stabilization for the anion and this point has never been experimentally verified.

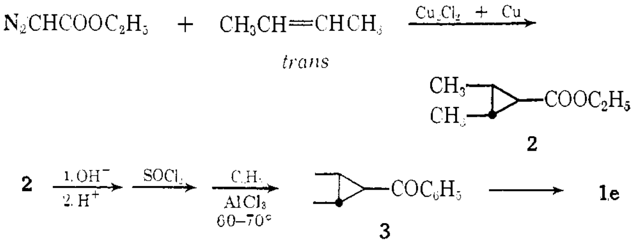
Although organometallic intermediates have provided a considerable amount of useful data about the interconversion of the cyclopropylcarbinyl and allylcarbinyl anionoid systems,[2,5,6] the rates of formation of such intermediates have not been previously used to gain more quantitative information. In the following study the relative rates of addition of isopropyllithium to various α-substituted styrenes to form the corresponding α-substituted benzyllithium reagents have been measured for several alkyl substituents and for the unsubstituted and alkyl-substituted cyclopropyl groups.

Results

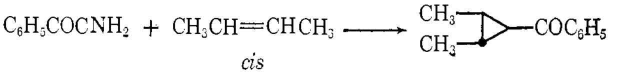
Starting Materials. The α-substituted styrenes used in this study were all prepared by the action of methylenetriphenylphosphorane on the corresponding ketones and, with the exception of **1c** and **1e**, have been previously reported.



The preparation and identification of the α-(*trans*-2-*cis*-3-dimethylcyclopropyl)styrene (**1e**) deserves more detailed consideration. The addition of ethyl diazoacetate to *trans*-2-butene in the presence of cuprous chloride and copper powder gave a low yield of ethyl



trans-2-*cis*-3-dimethylcyclopropanecarboxylate, which was converted to phenone **3** in 35% yield by the indicated sequence of reactions. In the nmr spectrum of **3**, the appearance of the proton adjacent to the carbonyl group as a doublet of doublets is only consistent for the *trans* arrangement of the two methyl substituents and should be contrasted with the observation of a triplet for this proton on the corresponding *cis* isomer prepared by Hammond[7] as indicated below. In addition, ketone **3** was homogeneous on a Polar UCON vpc column which has been reported to readily separate



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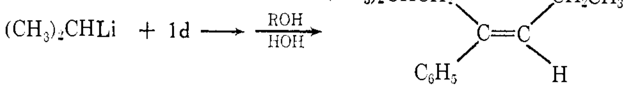
the three geometric stereoisomers of 2,3-dimethylcyclopropyl phenyl ketone.[8] Ketone **3** was then converted to olefin **1e** in an over-all yield of 73% by the Wittig reaction.

Addition Products. Although isopropyllithium in contact with vinylcyclopropane for 1 hr at −55° in diethyl ether does not undergo any detectable reaction, the addition of the lithium reagent to the α-substituted styrenes **1** was observed to take place readily under these conditions. The addition of isopropyllithium to **1a–c** followed by hydrolysis with aqueous ethanol produced only the expected hydrocarbons **5a–c**.

$$(CH_3)_2CHLi \ + \ 1 \xrightarrow{(C_2H_5)_2O} \xrightarrow[C_2H_5OH]{H_2O} C_6H_5(R)CHCH_2CH(CH_3)_2$$

5a, R = C_2H_5
b, R = $CH(CH_3)_2$
c, R = $CH(C_2H_5)_2$

However, the addition of isopropyllithium to α-cyclopropylstyrene (**1d**) under a variety of conditions listed in Table I, followed by hydrolysis or alcoholysis, resulted in the formation of 4-phenyl-2-methyl-*cis*-4-heptene (**6**). Under no circumstances was any 1-phenyl-1-cyclopropyl-3-methylbutane (**5**, R = c-C_3H_5) observed.



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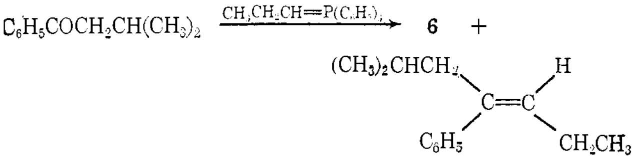
The assignment of stereochemistry was made by a consideration of the chemical shift value of the vinyl hydrogen triplet of **6** at τ 4.39 (*vide infra*). A mixture of the *cis* isomer **6** and the *trans* isomer **7** (65 and 35%, respectively) was prepared by the action of propylidenetriphenylphosphorane on 1-phenyl-3-methyl-1-butanone. An nmr spectrum of the mixture showed vinyl hydrogen triplets at τ 4.39 and 4.59. The τ 4.39 triplet



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[3] M. E. H. Howden and J. D. Roberts, *Tetrahedron Suppl.*, **2**, 403 (1963).

[4] R. J. Piccolini and S. Winstein, *ibid.*, **2**, 423 (1963).

[5] (a) J. D. Roberts and R. H. Mazur, *J. Am. Chem. Soc.*, **73**, 2509 (1951); (b) M. S. Silver, P. R. Shafer, J. E. Nordlander, C. Ruchardt, and J. D. Roberts, *ibid.*, **82**, 2646 (1960); (c) D. J. Patel, C. L. Hamilton, and J. D. Roberts, *ibid.*, **87**, 5144 (1965); (d) M. E. H. Howden, A. Maercker, J. Burdon, and J. D. Roberts, *ibid.*, **88**, 4261 (1966); (e) A. Maercker and J. D. Roberts, *ibid.*, **88**, 1742 (1966); (f) J. D. Roberts, E. R. Trumbull, Jr., W. Bennett, and R. Armstrong, *ibid.*, **72**, 3116 (1950).

[6] (a) G. Wittig and E. Hahn, *Angew. Chem.*, **72**, 781 (1960); (b) G. Wittig and J. Otten, *Tetrahedron Letters*, 601 (1963).

[7] D. O. Cowan, M. M. Couch, K. R. Kopecky, and G. S. Hammond, *J. Org. Chem.*, **29**, 1922 (1964).

[8] Cowan, Couch, Kopecky, and Hammond[7] observed that the copper salt catalyzed decomposition of diazoacetophenone in the presence of *trans*-2-butene produced an inseparable mixture of an unidentified unsaturated compound and ketone **3**, but the latter was not isolated pure, and the nmr spectrum was not reported.

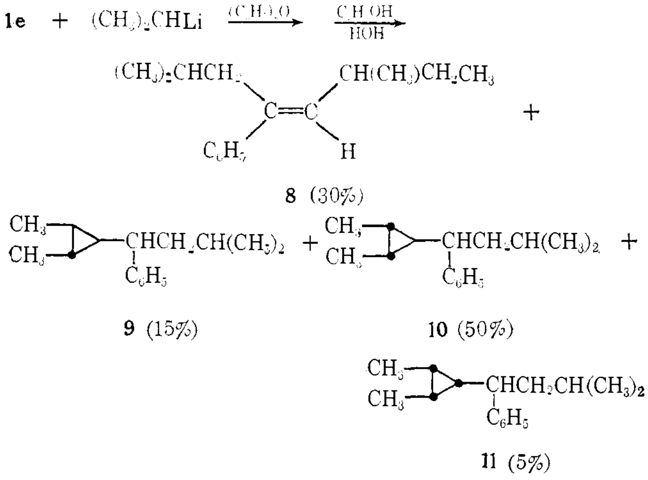
Table I. Effect of Varying Reaction Conditions on the Product Distribution for Isopropyllithium Addition to α-Cyclopropylstyrene (**1d**)

No.	Temp, °C	Reaction time, min	Solvent (%)	Method of work-up	Compd **1d**	Prod, **6**
1	−70	1	Ether	EtOH, −70°	83	17
2	−50	5	Ether	EtOH, −50°	2	93
3	−68	60	Ether	EtOH, −68°	20	80
4	−55	2.5	Ether-pentane (50:50)	CH_3OH, −55°	37	63
5	−55	20	Ether-pentane (20:80)	EtOH, −60°	55	44
6	−50	30	Ether-pentane (15:85)	EtOH, −50°	62.5	37.5
7	−70	15	Ether-pentane (10:90)	EtOH, −55°	50	0[a]
8	−65	5	Pentane	EtOH, −57°	100	0
9	−45	30	Tetrahydrofuran	H_2O, −40°	0	100
10	−45	30	Tetrahydrofuran-KBr	H_2O, −40°	0	100
11	−50	60	Ether with TMED[b]	EtOH, −45°	0	100

[a] Reference 22. [b] N,N,N′,N′-Tetramethylethylendiamine; ref 21.

was therefore assigned to the hydrogen *cis* to the phenyl group consistent with the expected diamagnetic anisotropic deshielding by the phenyl group in this isomer.[9] Fractional distillation of **6** and **7** achieved partial separation with an enrichment of the *trans* isomer in the lower boiling fraction consistent with the pattern observed by Cram[10] for olefins of similar structure.

The addition of isopropyllithium to α-(*trans*-2-*cis*-3-dimethylcyclopropyl)styrene (**1e**) gave, after hydrolysis, four products, **8–11**, all of which showed a strong parent ion at *m/e* 216 in the mass spectrum and gave a correct analysis for $C_{16}H_{24}$. Olefin **8** (*ca.* 30% of the product mixture) was isolated pure and identified by its infrared and nmr spectrum. Since the vpc and nmr data indicated the presence of only one geometrical isomer, the *cis* stereochemistry was assigned in analogy with the results for the addition of isopropyllithium to α-cyclopropylstyrene. The remaining three cyclopropyl isomers **9–11** were isolated as two fractions by preparative vpc and, although the gross structure was apparent from a consideration of elemental analysis, mass spectral, nmr, and infrared data (see Experimental Section), the stereochemistry of each individual isomer could not be unambiguously assigned. On the basis of the relative yields, 5, 15, and 50% of the total product mixture (in order of increasing elution times), and a consideration of steric interactions in the final structures, one would expect the associated structures to be **11**, **9**, and **10**, respectively, provided equilibration was complete, or nearly complete.[11]



8 (30%)

9 (15%)

10 (50%)

11 (5%)

Kinetic Data. The relative rates of addition of isopropyllithium to various α-substituted styrenes **1a–e** are indicated in Table II. Additions were carried out under pseudo-first-order conditions in the presence of an excess of isopropyllithium which was in the concentration range 0.5–1.5 *M*. The rate of disappearance of the starting olefin was followed by low-temperature transfer and hydrolysis of aliquots with subsequent vpc analysis in which a xylene peak or the total integrated area of the starting olefin plus the product peak was used as an internal standard. Typical data are tabulated in the Experimental Section and displayed in Figure 1. Relative rates were calculated by a comparison of the pseudo-first-order rate constants divided by the stoichiometric isopropyllithium concentration as determined by the usual double-titration procedure.[12] Although the state of aggregation of the active species of the isopropyllithium in ether is not definitely known, its concentration was assumed to be proportional to the stoichiometric concentration of isopropyllithium over the narrow range of concentrations used.[13–15]

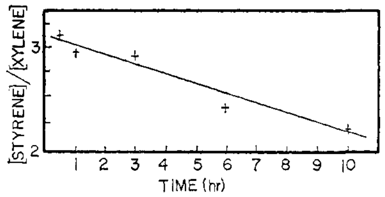


Figure 1. Rate plot for the addition of isopropyllithium to α-isopropylstyrene (**1b**) at −45° in diethyl ether. (For tabulated data and a discussion of errors see Experimental Section.)

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(9) The vinyl hydrogens *cis* and *trans* to phenyl in α-methylstyrene are found at τ 4.64 and 4.95, respectively: N. S. Bhacca, L. F. Johnson, J. N. Shoolery, "NMR Spectra Catalog," No. 232, Varian Associates, Palo Alto, Calif., 1962.

(10) D. J. Cram, *J. Am. Chem. Soc.*, 71, 3883 (1949).

(11) A study of product distribution as a function of time at −45° (Experimental Section) suggested that substantial equilibration had occurred.

(12) H. Gilman and J. W. Morton, *Org. Reactions*, **8**, 285 (1954).

(13) Z. K. Cheema, G. W. Gibson, and J. F. Eastham, *J. Am. Chem. Soc.*, **85**, 3517 (1963).

(14) F. A. Settle, M. Haggerty, and J. F. Eastham, *ibid.*, **86**, 2076 (1964).

(15) *n*-Butyllithium which exists as complexed dimers in ether solution has been shown to undergo reactions which are first order in the stoichiometric concentration of the lithium reagent.[16]

(16) J. F. Eastham and G. W. Gibson, *J. Am. Chem. Soc.*, **85**, 2171, (1963).

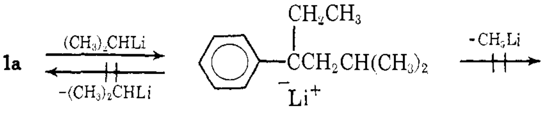
Table II. Rate Constants for the Addition of Isopropyllithium in Diethyl Ether to α-Alkylstyrenes at −45°

Alkyl group	Rate constant[a,b]	Detns	Rel rates
Ethyl (**1a**)	$(3.6 \pm 0.1) \times 10^{-4}$	3	28.0
Isopropyl (**1b**)	$(1.3 \pm 0.3) \times 10^{-5}$	3	1.0
3-Pentyl (**1c**)	$(7.7 \pm 0.1) \times 10^{-6}$ [c]	2	0.6
Cyclopropyl (**1d**)	$(4.0 \pm 1.3) \times 10^{-3}$	3	310
trans-2,3-Dimethylcyclopropyl (**1e**)	$(1.5 \pm 0.2) \times 10^{-3}$	2	115

[a] Pseudo-first-order rate constants normalized to the stoichiometric isopropyllithium concentration. [b] Unless otherwise specified rate data were obtained by vpc analysis with an internal *m*-xylene standard (see Experimental Section). [c] Vpc data were normalized to the sum of starting olefin and product areas.

Discussion

Products. That isopropyllithium readily added to styrenes **1a–c** to produce, after hydrolysis, exclusively hydrocarbons **5a–c**, respectively, in high yield, provides evidence against any reversibility of the addition under the conditions used. For example, the loss of methyllithium from an intermediate such as **12** should be even more favored than the loss of isopropyllithium and would lead to olefin **13** which would either be directly isolated or would undergo further addition by isopropyllithium.



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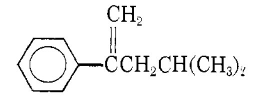

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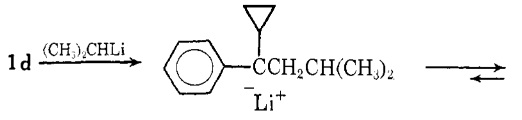
The result for isopropyllithium addition to α-cyclopropylstyrene (**1d**) requires more detailed consideration since only product **6** from hydrolysis of the allylcarbinyllithium **15** is formed and with the specific stereochemistry indicated.



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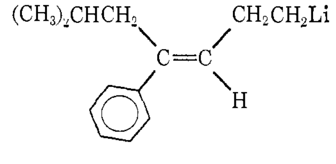

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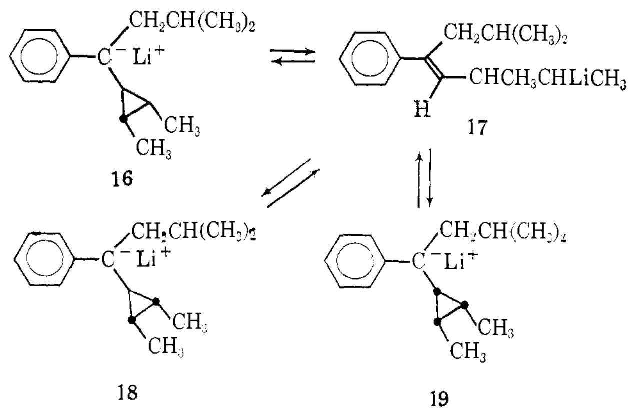
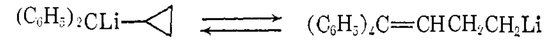
Indirect evidence for the suggested equilibrium between **14** and **15** can be found in the observation that the addition of isopropyllithium to closely related styrene **1e** produced, after hydrolysis, a mixture of isomeric products, **8–11**, which must have resulted from an equilibration of the open chain and cyclic alkyllithium species depicted in Scheme I. Because the allylcarbinyllithium **17** is a secondary lithium reagent, the over-all equilibrium, unlike that for **14** and **15**, lies more in favor of the ring-closed species **16**, **18**, and **19**.[17]

Scheme I



It should be noted that Roberts and Maercker[5e] have recently established the existence of a rapid reversible equilibrium (at 0°) between **20** and **21** which lies almost entirely in favor of the open-chain structure **21** in diethyl ether and the cyclic structure **20** in the more polar tetrahydrofuran.[18,19]



20 21

In an effort to shift the equilibrium between **14** and **15** more toward the benzylic lithium reagent, the addition of isopropyllithium was carried out in tetrahydrofuran (see Table I, No. 9 and 10) and in diethyl ether mixed with N,N,N′,N′-tetramethylethylenediamine (No. 11) which complexes strongly with the lithium and increases the ionic character of the bond,[21] but hydrolysis resulted only in the formation of olefin **6**.

Since previous workers[2] have shown that under conditions of very low temperature and low solvent polarity cyclopropylcarbinyllithium reagents can sometimes be trapped, several of the alkyllithium addition reactions to styrene **1d** were performed at temperatures down to −70° and in solvents varying from pure diethyl ether to pure pentane, but again only olefin **6** was isolated in those runs in which addition occurred.[22] No addition took place in pentane at −65°.

The use of stereomodels suggests that the predominant conformational isomer of α-cyclopropylstyrene

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(17) The preparation of the tetrahydropyranyl ether of 3-hydroxy-2-methylbutyltriphenylphosphorane which was unsuccessfully treated with isovalerophenone in an effort to ultimately synthesize alkyllithium **17** is described in the Experimental Section. Unconverted isovalerophenone was recovered from the reaction mixture.

(18) The observed shift to the benzylic lithium reagent in more polar solvents was attributed to an increase in the ionic character of the carbon–lithium bond. The use of potassium in place of lithium resulted in the exclusive formation of 1,1-diphenylcyclopropylcarbinylpotassium.[5c]

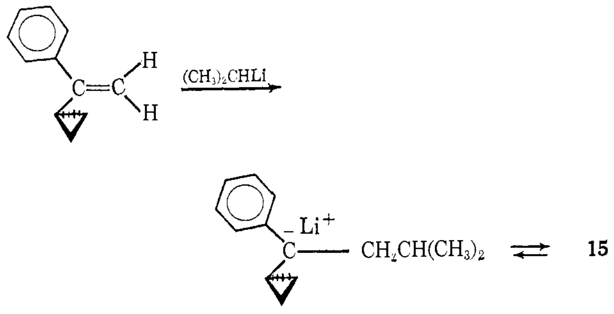
(19) Even allylcarbinylmagnesium bromide (in diethyl ether), a compound with a carbon–metal bond presumably with less ionic character than the carbon–lithium bond,[20] and with no phenyl substituent to stabilize the cyclopropylcarbinyl form, has been shown to be in equilibrium with the latter species.[6b]

(20) E. G. Rochow, D. T. Hurd, and R. N. Lewis, "Chemistry of Organometallic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1957, p 18.

(21) (a) C. G. Eberhardt and W. A. Butte, *J. Org. Chem.*, **29**, 2928 (1964); (b) C. G. Screttas and J. F. Eastham, *J. Am. Chem. Soc.*, **87**, 3276 (1965); (c) S. W. Langer, Jr., *Trans. N. Y. Acad. Sci.*, 27, 741 (1965).

(22) The residual oil from the alkyllithium addition carried out in 90% pentane and 10% diethyl ether (Table I, No. 7) contained 50% of a component boiling lower than styrene **1d** and tentatively identified from the nmr spectrum as phenylcyclopropylmethylmethane.

(**1d**) is that form in which the cyclopropane ring is oriented *anti* to the phenyl ring as shown below. Such a conformation avoids serious nonbonded interactions



14a

between the cyclopropane methylene groups and the *o*-hydrogen.[23] The addition of isopropyllithium to the rotamer described would result in the initial formation of alkyllithium **14a** in which the cyclopropane ring is still *anti* to the phenyl ring.

If the rate of rearrangement of **14a** to allylcarbinyllithium **15** is faster than the rate of equilibration of **14a** with the other possible rotational isomers, as is suggested by the isolation after hydrolysis only of products derived from **15**, then only *cis* isomer **15** should be formed. The presence of any rotational isomer of **14** in which the cyclopropane ring is either *skew* or *cis* to the phenyl group will lead to the formation of the rearranged lithium reagent with the opposite geometrical configuration to that of **15** and after hydrolysis to hydrocarbon **7** which was not an observed reaction product.

Rate Study. The relative facility of all of the addition reactions listed in Table II suggests that the primary driving force is the formation of a stabilized benzylic lithium reagent,[25] and one would presume that the transition state resembles such an intermediate. Although nonconjugated alkyllithium compounds are thought to be complexed dimers in ether[16] with a covalent carbon–lithium bond which is undoubtedly not a good approximation to a carbanion,[28] recent studies of the electronic absorption spectra[29a] and nmr spectra[29b,30] of benzyllithium and related structures in ethers have indicated that the benzylic carbon atom is probably sp^2 hybridized and possesses considerable negative charge character.

With the above considerations in mind it is instructive to note that the two cyclopropyl derivatives **1d** and **1e** added isopropyllithium approximately 200–300 times faster than the corresponding open-chain derivatives **1b** and **1c**, respectively. This result clearly implies that the cyclopropyl group is capable of providing considerable stabilization to the transition state for the addition process. Since the σ_m value for the cyclopropyl group, -0.102[31] or -0.07,[32] strongly indicates that cyclopropyl attached to an sp^2-hybridized carbon atom acts as a very weak electron donor and would therefore tend to destabilize an adjacent anionic center, the observed rate enhancement for this group relative to a simple alkyl group is undoubtedly dependent on homoallylic charge delocalization.

The substitution of methyl groups on the cyclopropane ring as in styrene **1e** reduces the observed rate constant by 63% relative to **1d**; the 3-pentyl derivative **1c** adds isopropyllithium at a rate which is 40% less than that for the addition to isopropylstyrene **1b**. Such decreases in rate are reasonable because of the expected inductive destabilization of the transition state by the methyl groups, and the effect should be larger for the cyclopropyl case both because cyclopropane is better able to transmit inductive effects compared to an sp^3-hybridized carbon–carbon bond[33] and because the previously discussed rate data does suggest some charge delocalization into the three-membered ring.

The higher reactivity of α-ethylstyrene (**1a**) over the isopropyl compound by a factor of 28 is not completely clear. If it is assumed that the rate difference is entirely due to the difference in inductive effects between isopropyl and methyl, then the use of the Taft σ^* values of -0.190 and -0.100 for the two substituents[34] allows one to calculate a ρ^* value for the addition reaction of $+14.4$, an unreasonably large value.[35] It must be assumed that the rate difference is primarily a manifestation of steric effects. Further studies are in progress.

Experimental Section[36]

1-Cyclopropylethanol. Cyclopropyl methyl ketone (50 g, 0.59 mole) was reduced to the alcohol with lithium aluminum hydride (12.5 g, 0.33 mole) in a modification of the method of Van Volkenburgh, Greenlee, Derfer, and Boord.[37] The yield was 17 g (0.20 mole) or 33% of the theoretical amount, bp 122–122.5° (lit.[45] bp 123.5°).

Vinylcyclopropane. The S-methyl xanthate of 1-cyclopropylethanol, prepared by the method of Benkeser and Hazdra,[38] was pyrolyzed[39] to give vinylcyclopropane, bp 40° (lit.[39] bp 40°) in a

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[23] A variety of evidence suggests that the preferred rotational isomer for vinylcyclopropane is the *s-trans* form.[24]

[24] (a) W. Luttke and A. de Meijere, *Angew. Chem. Intern. Ed. Engl.*, **5**, 512 (1966); (b) L. S. Bartell, *J. Chem. Phys.*, **32**, 827 (1960); (c) G. R. DeMare and J. S. Martin, *J. Am. Chem. Soc.*, **88**, 5033 (1966).

[25] With the exception of the addition of isopropyllithium and *t*-butyllithium to ethylene and propylene at −50° in diethyl ether observed by Bartlett, Friedman, and Stiles,[26] alkyllithium reagents do not add readily to nonconjugated or unstrained double bonds.[27]

[26] P. D. Bartlett, S. Friedman, and M. Stiles, *J. Am. Chem. Soc.*, **75**, 1771 (1953).

[27] J. E. Mulvaney and Z. G. Gardlund, *J. Org. Chem.*, **30**, 917 (1965).

[28] C. G. Screttas and J. F. Eastham, *J. Am. Chem. Soc.*, **88**, 5668 (1966).

[29] (a) R. Waack and M. A. Doran, *ibid.*, **85**, 1651 (1963); (b) R. Waack, M. A. Doran, E. B. Baker, and G. A. Olah, *ibid.*, **88**, 1272 (1966).

[30] R. B. Bates, D. W. Gosselink, and J. A. Kaczynski, *Tetrahedron Letters*, 205 (1957).

[31] Determined from the pK_a (5.90) of *m*-cyclopropylbenzoic acid in 50 vol. % aqueous ethanol at 25.0° by Dr. Ronald H. Rynbrandt.

[32] J. Smejkal, J. Jonas, and J. Furkas, *Collection Czech. Chem. Commun.*, 29, 2950 (1964).

[33] J. A. Landgrebe and D. E. Applequist, *J. Am. Chem. Soc.*, **86**, 1536 (1964).

[34] R. W. Taft, in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, Chapter 13.

[35] Values which exceed +5.0 have not been reported.

[36] All nmr spectra were measured in carbon tetrachloride with a Varian A-60 spectrometer. Chemical shifts are expressed on the τ scale. All infrared spectra were taken in carbon tetrachloride in sodium chloride cells on a Beckman IR-8 spectrophotometer. The polystyrene peak of 2849.0 cm^{-1} was used as standard. Boiling points are uncorrected. Elemental analyses were done at either Huffman Laboratories Inc., Wheatridge, Colo., or at Galbraith Laboratories, Louisville, Ky. Mass spectra were taken on a Nuclide Analysis Associates Model 12-90G. Vapor phase chromatography was done on either an Aerograph Hy-FI or an F & M Model 700 instrument both fitted with Barber Coleman recorders having Disc Integrators.

[37] R. Van Volkenburgh, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *J. Am. Chem. Soc.*, 71, 3595 (1949).

[38] R. A. Benkeser and J. J. Hazdra, *ibid.*, **81**, 228 (1959).

[39] C. G. Overberger and A. E. Borchert, *ibid.*, **82**, 4897 (1960).

15% yield based on alcohol. Vpc on an 8 ft × 0.25 in. diisodecyl phthalate column showed a single component.

α-Ethylstyrene (1a). Propiophenone (33.6 g, 0.251 mole) was converted to α-ethylstyrene (18.5 g, 0.14 mole, 56%) by the method of Ketley and McClanahan,[40] bp 70° (7 mm) [lit.[41] bp 73° (17 mm)].

α-Isopropylstyrene (1b). The desired olefin (21.5 g, 0.147 mole), bp 189° (lit.[42] bp 192°), was prepared in 59% yield by the previously stated method.[40]

3-Benzoylpentane. Potassium *t*-butoxide was prepared by the method of Johnson and Daub[43] from potassium (59.5 g, 1.52 g-atoms) and *t*-butyl alcohol (1.5 l. dried over calcium hydride for 12 hr at 50° and distilled). Acetophenone (60.7 g, 0.5 mole) was added (0.5 hr), and the resulting dark red solution was treated with ethyl iodide (193.3 g, 1.24 moles, 100 ml, purified by passage through an alumina column) at 40° for 1 hr and maintained at reflux for 20 hr during which a white solid precipitated. Water (100 ml) was added; the reaction mixture was distilled to remove most of the *t*-butyl alcohol, and water (1 l.) and ether (500 ml) were added. The ether layer was dried and worked up in the usual manner to give 3-benzoylpentane (21.9 g, 0.124 mole, 24.8%), bp 90° (1 mm) [lit.[44] bp 229° (710 mm)]. The nmr and infrared spectra were consistent with the assigned structure.

2-Phenyl-3-ethyl-1-pentene (1c). 3-Benzoylpentane (18.6 g, 0.106 mole) was converted to α-3-pentylstyrene (12.9 g, 0.074 mole, 70%) by the procedure previously described.[40] The product, bp 53° (0.5 mm), gave infrared absorptions at 3100–2880, 1690, 1625, 1600, 1575, 1490, 1460, 1380, 896, and 700 cm^{-1}. The nmr spectrum showed a broadened singlet at 2.78 (5 H), a doublet at 4.79 (1 H, J = 1.5 cps), a multiplet at 5.03 (1 H), a quintet at 7.62 (1 H, J = 6.5 cps), two quintets displaced by 1.5 cps and centered at ~8.5 (4 H, J = 6.5 cps), and a triplet at 9.12 (6 H, J = 6.5 cps) in perfect agreement with the assigned structure.

Anal. Calcd for $C_{13}H_{18}$: C, 89.47; H, 10.59. Found: C, 89.47; H, 10.59.

α-Cyclopropylstyrene (1d). The olefin was prepared from cyclopropyl phenyl ketone (Aldrich) by the method of Ketley and McClanahan[40] in 66.3% yield, bp 63° (2 mm) [lit.[40] bp 107° (25 mm)], λ_{max} 240 mμ (ϵ 10,500). The infrared and nmr spectra were consistent with the structural assignment.

Ethyl *trans*-2-*cis*-3-Dimethylcyclopropanecarboxylate (2). Yellow ethyl diazoacetate prepared by the method of Searle[45] was slowly added (8 hr) to a stirred suspension of copper powder (0.5 g) and cuprous chloride (1 g) in liquid *trans*-2-butene (56 g, 1 mole). After being stirred 8 hr, 80% of the *trans*-2-butene was recovered by distillation, and the residue was vacuum distilled to give ethyl *trans*-2-*cis*-3-dimethylcyclopropancarboxylate (9.5 g, 6.7% yield), bp 152°. The infrared spectrum showed absorptions at 3025–2860, 1715, 1440, 1375, 1360, 1340, 1170, 1150, 1085, 1050, and 1025 cm^{-1}. The nmr spectrum showed a quartet at 5.96 (2 H, J = 7 cps) and a triplet at 8.78 (J = 7 cps) overlapping a multiplet at 8.5–9.2 (12 H). Bestman and Seng[46] report bp 167° for an unknown isomer(s) of ethyl 2,3-dimethylcyclopropanecarboxylate.

***trans*-2-*cis*-Dimethylbenzoylcyclopropane (3).** Ethyl *trans*-2-*cis*-3-dimethylcyclopropanecarboxylate (50.7 g, 0.356 mole) was heated at reflux with 150 ml of 10% sodium hydroxide solution. The solution was acidified, extracted with ether (200 ml), saturated with sodium chloride, and further extracted with ether (100 ml). The combined extracts were dried over sodium sulfate and evaporated to give *trans*-2-*cis*-3-dimethylcyclopropanecarboxylic acid. The nmr spectrum of the crude material showed a singlet at −0.95 (1 H) and a doublet (J = 7 cps) superimposed on a more complex multiplet at 8.84 (9 H).

The crude red acid was treated with thionyl chloride (60 g, 0.5 mole) for 2 hr at 90° followed by distillation to give *trans*-2-*cis*-3-dimethylcyclopropylcarbonyl chloride (38 g, 0.286 mole, 80%).

To 250 ml of benzene and 38.8 g (0.287 mole) of aluminum chloride at 80° was added the acid chloride (45 min), and the stirred solution was kept at 60 to 70°[47] both during the addition and for the following hour, after which the mixture was poured onto 1 l. of ice. Solid potassium hydroxide was added until the heavy precipitate dissolved. The benzene layer was separated, washed with 5% hydrochloric acid (200 ml) and two 100-ml portions of sodium bicarbonate solution, dried over sodium sulfate, and evaporated to give a residue which was distilled, bp 69° (0.17 mm). The *trans*-2-*cis*-3-dimethylcyclopropyl phenyl ketone (16 g, 0.092 mole, 35% based on crude acid chloride) gave an infrared spectrum with prominent bands at 3090–2880, 1680, 1670, 1600, 1580, 1450, 1382, 1358, 1020, and 1000 cm^{-1} among others. The nmr spectrum showed complex multiplets centered at τ 2.1 (2 H) and 2.5 (3 H, C_6H_5CO), a doublet of doublets 7.65 (1 H, COCH), and a doublet at 8.89 (J = 3–4 cps) superimposed on a more complex group of absorptions at *ca.* 8.27–9.38 (total 8 H).

α-(*trans*-2-*cis*-3-Dimethylcyclopropyl)styrene (1e). *trans*-2-*cis*-3-Dimethylcyclopropyl phenyl ketone (14 g, 0.08 mole) was converted to the corresponding styrene (10 g, 0.058 mole, 73% yield), bp 64° (1 mm), by the method previously described.[40] The infrared spectrum showed prominent absorptions at 3090–2860, 1620, 1585, 1565, 1480, 1440, 1380, 1065, 1025, and 888 cm^{-1}. The ultraviolet spectrum showed λ_{max} 243.5 mμ (ϵ 11,500) (Beckman DB, cyclohexane). The mass spectrum showed M^+ 172 and $(M + 1)^+$ 173 (14%) consistent with $C_{13}H_{16}$. The nmr spectrum showed a complex phenyl absorption at 2.4–2.95 (5 H), broad singlets at 4.58 (1 H) and 5.12 (1 H, C=CH$_2$), and a complex absorption from *ca.* 8.2 to 9.4 (9 H).

Anal. Calcd for $C_{13}H_{16}$: C, 90.64; H, 9.36. Found: C, 90.71; H, 9.30.

Isopropyllithium in ether was prepared by a modification of the method of Gilman[12] which included the use of argon instead of nitrogen as the inert atmosphere and Dry Ice–kerosene bath. All glassware used for handling reagents or for the reaction was dried in a 100° oven for 8 hr before use. The ether was stored over calcium hydride, distilled from calcium hydride, and stored over sodium. The isopropyl chloride was distilled from calcium hydride within 1 hr before use.

In a typical preparation, 85 ml of ether was put into a 100-ml reaction flask; the stirrer and argon flow were started, and 2 g (0.298 g-atom) of lithium wire (2% sodium) was flattened and cut directly into the flask with scissors. The flask was cooled to −35°, and a mixture of 11 ml (0.12 mole) of isopropyl chloride and 40 ml of ether was added slowly at that temperature. The reaction started after the addition of about 10 ml of the isopropyl chloride solution. One hour after the reaction had ceased to be exothermic, the temperature was lowered to −45°. It was maintained there for 6 hr and at −60° overnight.

The concentration of the solution was then determined to be 0.767 M (*ca.* 86% yield by double titration).[12] The concentration of the solution prepared could be regulated over the range from 0.5 to 2 M by adjusting the amounts of reagents and solvent used. The solutions were not filtered but were transferred rapidly by means of large syringes.

Isopropyllithium in tetrahydrofuran was prepared and its concentration determined exactly as in the previous procedure except for the substitution of a stainless steel high-speed stirrer for the tantalum Hershberg stirrer used in ether.

Isopropyllithium in Pentane.[12] The apparatus used was the same as was used for isopropyllithium in ether except that a reflux condenser was substituted for the low-temperature thermometer. In a typical preparation, 200 ml of pentane was used in a 500-ml reaction flask. The lithium (2.3 g, 0.33 g-atom) was used as before and the solvent heated to reflux. A mixture of 15 ml (12.9 g, 0.16 mole) of isopropyl chloride and 100 ml of pentane were placed in the addition funnel and added over 10 min. After a 24-hr reflux period, the concentration was determined by direct titration of an aliquot of this solution in water to be 0.374 M. This represents about 70% of the theoretical amount of isopropyllithium. The solutions in pentane were usually transferred by syringe.

Attempted Addition of Isopropyllithium in Ether to Vinylcyclopropane. Vinylcyclopropane (0.5 g, 0.007 mole) in ether (25 ml) was slowly added (1 hr) to a stirred solution of isopropyllithium in (45 ml, 0.672 M) which was maintained at −55° under an argon

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[40] A. D. Ketley and J. L. McClanahan, *J. Org. Chem.*, **30**, 942 (1965).

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[42] C. G. Overberger and D. Tanner, *J. Am. Chem. Soc.*, **77**, 369 (1955).

[43] W. S. Johnson and G. H. Daub, *Org. Reactions*, **6**, 42 (1951).

[44] W. H. Perkin, *J. Chem. Soc.*, **45**, 184 (1884).

[45] N. E. Searle in "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, Ed., John Wiley and Sons, Inc., New York, N. Y., 1963, p 424.

[46] H. J. Bestman and F. Seng, *Angew. Chem.*, **74**, 154 (1962).

[47] The use of a reaction temperature ≤60° results in a mixture of the desired product **3** and an unsaturated ketone. The mixture was inseparable by distillation or by several vpc columns (Carbowax 20M, Polar UCON, SE-30, QF-1). It is likely that the impurity is the same as that reported by Cowen, Couch, Kopecky, and Hammond[7] in their preparation of **3**. Addition of aluminum chloride to a mixture of the acid chloride and benzene gave a lower yield (*ca.* 25%).

atmosphere. Water was added at −55°, and the solution was warmed after the ether had become clear. More water was added, and the ether was separated, washed with 10% ammonium chloride solution, 5% sodium bicarbonate solution, and water and dried over sodium sulfate. Vpc (8-ft diisodecyl phthalate, 25°) and an nmr spectrum showed only ether and unreacted starting materials.

4-Phenyl-2-methylhexane (5a). α-Ethylstyrene (1.8 g, 0.0136 mole) was added to isopropyllithium in ether (40 ml, 0.705 *M*) at −30° in an argon atmosphere. After 8 hr, the stirred solution was hydrolyzed with 10 ml of 95% ethanol at −30°, warmed to 25°, and treated with an additional 25 ml of water. After the usual work-up, the oil was distilled to give 4-phenyl-2-methylhexane (1.0 g, 0.063 mole, 46% yield), bp 55° (0.8 mm). The infrared spectrum showed prominent absorptions at 3040 (w), 2970, 2930, 2880, 1600 (w), 1490, 1460, 1450, 1380, and 1370 cm^{-1}. The nmr spectrum showed a broad singlet at 2.85 (5 H), a broad multiplet at 7.6 (1 H), a complex absorption at 8.1–8.9 (5 H), and a complex absorption at 9.05–9.5 (9 H).

Anal. Calcd for $C_{13}H_{20}$: C, 88.56; H, 11.43. Found: C, 88.32; H, 11.43.

3-Phenyl-2,5-dimethylhexane (5b) was prepared from α-isopropylstyrene (2.667 g, 0.0183 mole) by the same procedure used for the preparation of 4-phenyl-2-methylhexane except that the reaction mixture was maintained at −32° for 8 hr, −70° for 13 hr, −35° for 2 hr, and −15° for 2 hr. The nmr spectrum indicated complete conversion to the desired product (1.4 g, 0.0074 mole, 40% yield), bp 52° (0.6 mm). The infrared spectrum showed prominent absorptions at 3080 (w), 3060 (w), 3020, 2960, 2920, 2860, 1595 (w), 1490, 1462, 1450, 1380, and 1360 cm^{-1}. The nmr spectrum showed a broad singlet at 2.87 (5 H), a multiplet at 7.4–7.9 (1 H), a complex absorption at 8.0–8.9 (4 H), and the mass spectrum gave M$^+$ 190.

Anal. Calcd for $C_{14}H_{22}$: C, 88.35; H, 11.65. Found: C, 88.53; H, 11.51.

4-Phenyl-2-methyl-5-ethylheptane (5c) was prepared from 2-phenyl-3-ethyl-1-pentene (4.0 g, 0.023 mole) by the method described above (90% conversion). The product was distilled to yield 1.65 g (0.0076 mole, 33%) of pure 4-phenyl-2-methyl-5-ethylheptane, bp 72° (0.25 mm), which gave M$^+$ 218. The infrared spectrum showed prominent absorptions at 3080 (w), 3050 (w), 3020, 2940, 2860, 1590, 1487, 1460, 1445, 1375, and 1360 cm^{-1}. The nmr spectrum showed a broad singlet at 2.88 (5 H), a broad multiplet at 7.4 (1 H), and a complex absorption at 8.2–9.55 (20 H).

Anal. Calcd for $C_{16}H_{26}$: C, 88.00; H, 12.00. Found: C, 87.79; H, 11.86.

4-Phenyl-2-methyl-*cis*-4-heptene (6). α-Cyclopropylstyrene (3.9 g, 0.027 mole) was added to isopropyllithium in ether (60 ml, 1.26 *M*) at −60° under argon. After 25 min the mixture was hydrolyzed at −40° with ethanol. The nmr spectrum indicated 93% conversion to the product olefin **6**. The final product (3.0 g, 0.0159 mole, 59% yield) showed infrared absorptions at 3100–2880, 1600 (w), 1495, 1465, 1430 (sh), 1385, and 1370 cm^{-1}. The nmr spectrum showed a multiplet at 2.8 (5 H), a triplet at 4.37 (1 H, J = 7 cps), a doublet at 7.56 superimposed on a quintet at 7.8 (4 H, J = 7 cps), a partly visible nonet at 8.4 (~1 H, J = 7 cps), and a triplet at 8.98 superimposed on a doublet at 9.18 (9 H, J = 7 cps).

Anal. Calcd for $C_{14}H_{20}$: C, 89.29; H, 10.71. Found: C, 89.48; H, 10.53.

4-Phenyl-2-methyl-4-heptene. A mixture of the *cis* and *trans* isomer (65:35) was prepared by a Wittig reaction[40] between 1-phenyl-3-methyl-1-butanone (35 g, 0.215 mole), which had been prepared in 70% yield by a Friedel–Crafts reaction,[48] and *n*-propyltriphenylphosphonium bromide (83.5 g, 0.217 mole). Because the olefins could not be separated from residual ketone by distillation, the mixture was subjected to lithium aluminum hydride reduction and distilled to give three fractions each of which contained a different ratio of the *cis* and *trans* olefins. Fractions which contained alcohol were treated with more lithium aluminum hydride and redistilled. The total olefin yield was 7.18 g (0.0038 mole) of 18%. The nmr spectrum of the mixtures showed among other absorptions vinyl triplets at 4.39 and 4.59 (J = 7 cps) (see Discussion).

Attempts to Detect 1-Phenyl-1-cyclopropyl-3-methylbutane from the Addition of Isopropyllithium to α-Cyclopropylstyrene (1d). The addition of isopropyllithium to α-cyclopropylstyrene was performed under the conditions shown in Table I (Discussion). The additions in mixed solvents were carried out by adding one solvent to the isopropyllithium prepared in the other solvent. In reaction 10, 3.5 g of potassium bromide was added to the isopropyllithium solution in THF before the addition of the starting material. In reaction 11, N,N,N′,N-tetramethylethylenediamine[21] was added to make its concentration equal to that of the isopropyllithium.

Addition of Isopropyllithium to α-(*trans*-2-*cis*-Dimethylcyclopropyl)styrene (1e). A 0.952 *M* solution of isopropyllithium in ether (50 ml) was placed in the usual apparatus at −45°, and 2.9 g (0.169 mole) of the styrene **1e** was added. The solution was stirred for 3 hr, and then 25 ml of water was added dropwise. The mixture was allowed to come to room temperature after hydrolysis, and the ether layer was separated and worked up in the usual manner. The product was shown to consist of four components by vpc (8-ft Carbowax 20M, 200°) which could not be separated by distillation, bp 63° (0.32 mm). A 15% QF-1 vpc column (0.5 in. × 10 ft) separated 1-μl samples cleanly into the four components but would not separate larger samples. The material was collected in three fractions from a 12% SE-30, 8% E-600 column (20 ft × 0.25 in.). The first two components were collected as one fraction and the the other two were obtained pure. The third component (fraction 2) was about 60% of the total. All fractions showed M$^+$ at *m*/*e* 216 and (M + 1)$^+$ at *m*/*e* 217 (17%) consistent with $C_{16}H_{24}$. In the case of the first fraction, the M$^+$ was more than five times the intensity of any peak of *m*/*e* over 58 and was the base peak. Since the ratio of the two components in this fraction was 30:70 by vpc (QF-1) the two components are hydrocarbons of mass 216 (see elemental analyses).

The infrared spectra of both fraction 1 and fraction 2 showed significant absorptions at 3080–3875, 1595, 1490, 1450, 1380, and 1360 cm^{-1}. The nmr spectrum of fraction 1 showed a broad singlet at 2.88 (5 H), and complex multiplets extending from 7.7 to 9.6 (19 H); a tall doublet (J = 6–7 cps) protruded at 9.17. Similarly the nmr spectrum of fraction 2 showed a broad singlet at 2.87 (5 H), and complex multiplets extending from *ca.* 7.7 to 9.8 (19 H). The infrared spectrum of fraction 3 showed significant absorptions at 3100–2880, 1590, 1490, 1460, 1390, and 1370 cm^{-1}. The nmr spectrum showed a singlet broadened at the base at 2.8 (5 H), a doublet at 4.63 (1 H, J = 9 cps), a doublet (J = 7 cps) superimposed on a smaller multiplet at *ca.* 7.65 (3 H), and a complex group of multiplets extending from *ca.* 8.2–9.2 (15 H); doublets (J = 7 cps) were clearly discernible at 9.0 and 9.15. The assignment of structures **11**,**9**; **10**; and **8** to fractions 1, 2, and 3 is discussed in the section on Results.

Anal. Calcd for $C_{16}H_{24}$: C, 88.82; H, 11.18. Found: Fraction 1: C, 89.03; H, 11.07. Fraction 2: C, 88.92; H, 11.10. Fraction 3: C, 88.05; H, 10.97.

Appearance of Products of the Addition of Isopropyllithium to α-(*trans*-2-*cis*-3-Dimethylcyclopropyl)styrene (1e). A 0.767 *M* solution of isopropyllithium in ether (30 ml) was placed in the same apparatus as before, and the temperature was adjusted to −45°. The substituted styrene **1e** (4 ml, 0.021 mole) was added, and the solution was stirred for 4 hr at −45°. Aliquots (5 ml) were removed by syringe 10, 30, and 60 min after addition of the styrene, and each was run into a stirred mixture of 25 ml of ice water and 20 ml of ether. The ether layer was then separated, dried over sodium sulfate, and evaporated. After 4 hr the remainder of the solution was worked up as in the previous experiment. The four samples were then examined by vpc (Hy-FI, 8-ft Carbowax 20M column 200°). The disappearance of the starting material and appearance of the products were followed (Table III). The peaks were not completely separated on the chromatogram so a line was dropped from the lowest point in the saddle between peaks to the base line of the chart. All peak areas were normalized to the total area.

Table III. Product Distribution as a Function of Time in the Addition of Isopropyllithium to Styrene (**1e**)

Sample	Time, min	Starting material remaining, %	Products, % 1	2	3	4
1	10	39.12	0.73	7.74	33.87	18.54
2	30	13.31	1.71	12.17	47.91	24.90
3	60	0.46	3.94	14.58	53.01	28.01
4	240	0	3.28	18.74	62.76	15.22

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[48] A. I. Vogel, "A Textbook of Practical Organic Chemistry," Longmans, Green, and Co., London, 1956, p 729.

General Method of Rate Study of the Addition of Isopropyllithium to α-Substituted Styrenes. A weighed sample of the styrene and 50 μl of spectroquality *m*-xylene were dissolved in 5 ml of dry ether. A solution of isopropyllithium in ether (0.5–1.5 *M*) was prepared and the concentration determined by double titration. The lithium reagent (35 or 40 ml) was placed in an oven-dried 50-ml, three-necked flask fitted with an argon inlet, a Trubore stirrer with Teflon paddle, and a low-temperature thermometer. The stirrer paddle was cut so that it would not interfere with the thermometer.

Several 5-ml syringes fitted with large-bore needles were dried in an oven for at least 1 hr and then placed in a vacuum desiccator before use. The desiccator had a 2-in. layer of Dry Ice in the bottom, a pierced porcelain plate on the ice, the syringes on the plate, and a heat shield of aluminum foil over the syringes. This would cool the syringes to below −20° in a very dry atmosphere. The isopropyllithium solution was cooled to −48°; the styrene mixture was added, and the temperature was adjusted to 45°. At intervals, 5-ml aliquots were withdrawn quickly with the syringes and injected through aluminum foil caps into 30-ml beakers. The beakers contained 5 ml of ether, 1 ml of 95% ethanol, and a magnetic stirring bar. The contents were cooled and stirred in a Dry Ice–acetone bath for 2 min before and 1 min after the addition of the aliquots. The beakers were allowed to come to room temperature and 15 ml of water was added with stirring. The ether layer was separated, extracted with 10 ml of water and then put in a numbered 10-ml flask for analysis.

The samples were examined on an F & M Model 700 chromatograph with a flame ionization detector. The elapsed time, amount of standard and starting material (SM) in disk integrator counts, and the quotient of starting material divided by standard were tabulated. In a few cases the standard was taken as the sum of starting material and product. A graph of log (starting material/standard) *vs.* time was prepared and the vertical uncertainty of a point was estimated by assuming a probably error of ±2 integrator counts in each vpc measurement. The best straight line was drawn by a visual estimate since the number of points in a given run (4 or 5) did not justify a more elaborate least-squares treatment. In general it was found that the later points in a run tended to be less accurate than the earlier ones even in those runs in which this could not be ascribed to vpc error. This is felt to be a result of deterioration of reaction conditions since water or oxygen entering the flask could destroy part of the lithium reagent and/or changes could occur in the reaction temperature especially during a run of many hours duration. All rate data were obtained at −45 ± 5° except those obtained at reaction times greater than 6 hr for which the error was ±15°.

The rate constants were calculated from the equation $k = 0.693/t_{1/2}$ for those reactions which were followed for more than one half-life. Rate constants for all other runs were determined by taking measurements of (starting material/standard) from the graph, *vide infra*, at two convenient times and applying the equation, $k = [2.303\Delta \log (\text{starting material/standard})]/\Delta t$. All rate constants were normalized to the concentration of isopropyllithium used in that run. Data from a typical run are given in Table IV (see Figure 1) for the addition of isopropyllithium to α-isopropylstyrene. The initial reaction mixture consisted of 0.146 g (0.001 mole) of α-isopropylstyrene in 40 ml of 0.726 *M* isopropyllithium in ether which contained 50 μl of *m*-xylene.

Table IV[a]

Time, hr	Xylene	SM	SM/xylene
0.0	. . .	. . .	3.17
0.5	66	208	3.15
1.0	126	370	2.94
3.0	136	390	2.87
6.0	125	297	2.38
10.0	146	320	2.17

[a] $k = (\ln 3.17 - \ln 2.17)/(3.6 \times 10^4\ \text{sec})(0.726\ \text{mole/l.}) = 1.46 \times 10^{-5}$ l. mole^{-1} sec^{-1}.

4-Tosyloxy-2-methyl-2-butanol. 3-Methyl-4-hydroxy-2-butanone (20 g, 0.2 mole) was dissolved in dry pyridine (130 ml) and cooled to 10°, and *p*-toluenesulfonyl chloride (55.5 g, 0.292 mole) was added over a 1-hr period after which the solution was stirred at 10° for 3 hr. Ether (100 ml) and 8 *M* hydrochloric acid (200 ml) were added, and the water layer was further extracted with two 50-ml portions of ether. The ether extracts were washed with water (200 ml), 5% sodium bicarbonate solution (200 ml), and water (200 ml) and dried over sodium sulfate.

The ether solution of the tosylate was added dropwise to a stirred suspension of sodium borohydride (4 g, 0.106 mole) in 95% ethanol (20 ml) and ether (25 ml) at 0° in an argon atmosphere. After 2 hr, ethanol (25 ml) was added, the reaction mixture was stirred for an additional 6 hr, and 1.2 *M* hydrochloric acid (200 ml) was slowly introduced. An ether extract was washed in the usual manner, dried over sodium sulfate, and evaporated to give the crude product which was used directly in the next step.

The infrared spectrum showed prominent absorptions at 3500 (broad), 2980–2880, 1590, 1450, and 1350 cm^{-1}. The nmr spectrum showed an A_2B_2 pattern centered at 2.5 (4 H), complex multiplets 5.83–6.7 (3 H), a singlet at 7.18 (1 H), a singlet at 7.60 (3 H), a complex multiplet at ~8.05–8.5 (1 H), and two doublets at 8.95 and 9.18 (6 H, J = 7 cps).

4-Bromo-3-methyl-2-butanol. The crude tosylate product from the previous reaction was added (solution in 50 ml of acetone) to lithium bromide (43.3 g, 0.5 mole) in dry acetone (150 ml), and the solution was maintained at reflux for 6 hr, cooled, mixed with water (1 l.), and extracted with ether (200 ml). The ether layer was worked up in the usual manner to produce a residue which was distilled to give 4-bromo-3-methyl-2-butanol (8.0 g, 0.0476 mole, 23.8% yield based on 3-methyl-4-hydroxy-2-butanone), bp 60° (1 mm). A second reaction gave a 38% yield.

The infrared spectrum showed significant absorptions at 3620, 3400 (broad), and 2980–2870 cm^{-1}. The nmr spectrum showed multiplets from 5.9 to 7.05 (4 H), a multiplet at 7.8–8.5 (1 H), and multiplets at 8.75–9.1 (6 H). The complexity of the spectrum was attributed to the presence of more than one diastereomer.

Anal. Calcd for $C_5H_{11}BrO$: C, 35.95; H, 6.64; Br, 47.83; O, 9.58. Found: C, 35.85; H, 6.60; Br, 47.71.

4-Bromo-3-methyl-2-butanol Tetrahydropyranyl Ether. 4-Bromo-3-methyl-2-butanol (80 g, 0.48 mole) was converted to the tetrahydropyranyl ether by the method of Ott, Murray, and Pederson.[49] The product (130 g, 0.516 mole, *ca.* 100% yield) was not purified further. The nmr spectrum showed a broad absorption at 5.35 (1 H), complex multiplets at 5.88–6.94 (5 H), complex multiplets at 7.8–8.65 (7 H), and complex multiplets at 8.7–9.1 (6 H).

Tetrahydropyranyl Ether of 3-Hydroxy-2-methylbutyltriphenylphosphonium Bromide. The crude ether from the previous experiment (130 g, 0.516 mole) was heated at 90° for 14 days with triphenylphosphine (200 g) in toluene (600 ml).[50] Every 48 hr the flask was cooled and the precipitated tan solid removed and washed with ethanol until it was white. The total yield of salt was 100 g (0.194 mole, 37.5%).

Attempted Preparation of the Tetrahydropyranyl Ether of 7-Hydroxy-4-phenyl-2,6-dimethyl-4-octene. The dry phosphonium salt from the previous reaction (20 g, 0.039 mole) was suspended in ether (100 ml) to which 1.06 *N* *n*-butyllithium in ether (41 ml, 0.043 mole) was added at −10° under an argon atmosphere. The dark red solution was allowed to warm to 25° and after 30 min, 6.6 ml (6.35 g, 0.039 mole) of isovalerophenone was introduced by syringe through a rubber septum on one neck of the reaction flask. The mixture became lighter in color and was maintained at reflux for 16 hr, after which it was worked up in the usual manner to give a crude product which was shown by the nmr spectrum to be almost pure starting ketone.

The reaction was repeated except that a twofold excess of *n*-butyllithium and a 1.4-fold excess of the ketone were used. One hour after the addition of the ketone, dry tetrahydrofuran was added, and the diethyl ether was removed by distillation. After a period of reflux at 63°, the reaction mixture was worked up, but only starting ketone and a small amount of 4-phenyl-2-methyl-4-octanol (tentatively identified) were isolated.

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