The Coupling Reaction of Phenyllithium with Allylic Chlorides. The Influence of Methyl Substituents on the Distribution of Products[1a,b]

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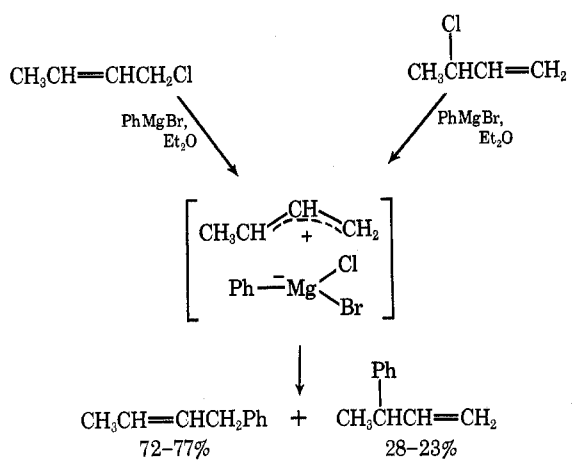
The reaction of phenyllithium with each of the possible mono- and dimethyl-substituted allylic chlorides is reported. Included are chlorides in which the termini of the allylic system are made distinguishable by ^{2}H or ^{14}C labels [3-chloro-2-methyl-1-propene and 4-chloro-*trans*- (or *cis*-) -2-pentene], although numerous attempts to prepare the latter compound exclusively tagged at one position were unsuccessful. The distribution of coupling products from the reaction with phenyllithium is discussed with respect to the influence of α-, β-, or γ-methyl substituents on the position of attack. The total preservation of double bond geometry when *trans*- or *cis*-1-chloro-2-butene and *trans*- or *cis*-1-chloro-2-methyl-2-butene undergo α attack is used to argue against previously proposed ion-pair and radical-pair mechanisms. The nonidentical product distributions from pairs of allylic isomers stand in contrast to earlier reports and are also most simply interpreted in terms of a concerted process.

Allylic halides couple with a wide variety of organometallic reagents, and several distinct mechanisms have been proposed. The first reasonable scheme was put forth by Wilson, Roberts, and Young[2] to explain the nearly identical distribution of products from reaction of phenylmagnesium bromide with either α- or γ-methylallyl chloride. They suggested that coordination of magnesium with chlorine sufficiently weakens the C–Cl bond that an ion-pair intermediate with almost no memory of its origin is formed; this intermediate then collapses to the two products (Scheme I). Reac-

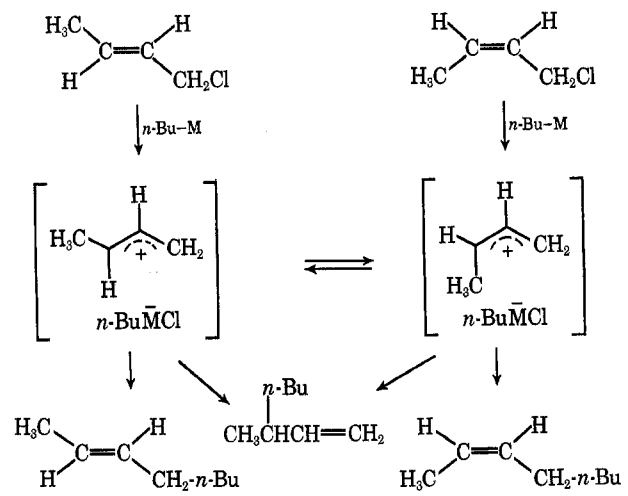
SCHEME I



tion of the same two chlorides with phenyllithium in ether similarly was reported to produce identical product mixtures consisting of about 90% crotylbenzene and 10% α-methylallylbenzene; the ion-pair mechanism was, again, invoked.[3]

More recently, Czernecki, *et al.*,[4] presented a detailed study of the reactions of *cis*- and *trans*-crotyl chloride and α-methylallyl chloride with *n*-butyllithium, *n*-butylsodium, and *n*-, *sec*-, and *tert*-butylmagnesium bromide. They concluded that all of the organometallic reagents produce products by the same general mechanism: heterolysis of the C–Cl bond by coordination to the metal followed by collapse of the ion pair to products (Scheme II). Differences between

SCHEME II



the various reagents were attributed to a delicate interplay of two factors: the relative electrophilicity of the metal (increasing from sodium to lithium to magnesium) and the relative nucleophilicity of the butyl group (decreasing along this series). In particular, with Grignard reagents the ion-pair intermediate is presumed to be longer lived and capable of bond rotation, thereby allowing partial loss of double bond geometry in the products from *cis*- and *trans*-crotyl chloride; with the lithium and, especially, sodium reagents, more rapid collapse to products results in essentially no loss of double bond stereochemistry. Differences in product distributions from the three chlorides were also interpreted within this framework.

A variation of this ion-pair mechanism was offered by Wawzonek, *et al.*,[5] to account for the purported loss of double bond integrity in the products from *cis*- and *trans*-crotyl chloride with phenyllithium and phenylsodium. In their view, the ion pair can return to covalent chloride and, to the extent that α-methylallyl chloride is thus generated, both *cis*- and *trans*-crotylbenzene are expected (Scheme III). The rather high activation energy for rotation about the partial

(1) (a) A portion of this work has appeared in preliminary form: R. M. Magid and R. D. Gandour, *J. Org. Chem.*, **35**, 269 (1970). (b) Partial support of this work by the Robert A. Welch Foundation is gratefully acknowledged, as is the assistance of the National Science Foundation in the purchase of a Varian Associates A-56/60A nmr spectrometer. (c) To whom inquiries should be addressed at the Department of Chemistry, The University of Tennessee, Knoxville, Tenn. 37916.

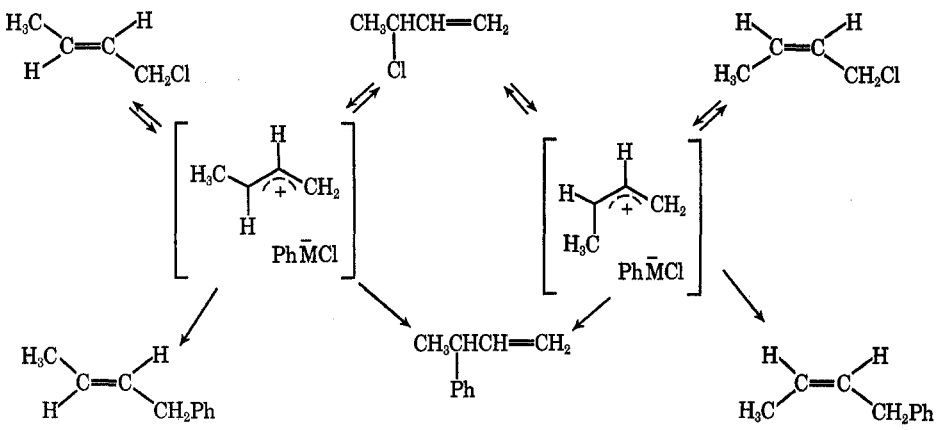
(2) K. W. Wilson, J. D. Roberts, and W. G. Young, *J. Amer. Chem. Soc.*, **71**, 2019 (1949).

(3) S. J. Cristol, W. C. Overhults, and J. S. Meek, *ibid.*, **73**, 813 (1951).

(4) S. Czernecki, C. Georgoulis, B. Gross, and C. Prevost, *Bull. Soc. Chim. Fr.*, 3713 (1968).

(5) S. Wawzonek, B. J. Studnicka, and A. R. Zigman, *J. Org. Chem.*, **34**, 1316 (1969).

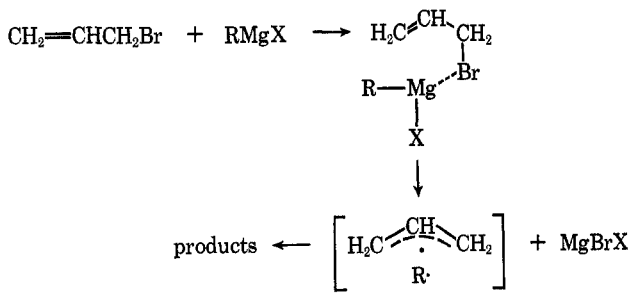
SCHEME III



double bond of long-lived allylic cations in strongly ionizing media[6] would probably argue against Scheme II and for this variation.

A distinctly different sort of mechanism was suggested by Gough and Dixon[7] for the coupling of allyl bromide with Grignard reagents. Based upon relative rate data, isolation and characterization of several minor products, and detection of an esr signal, a radical-pair intermediate was put forth (Scheme IV).

SCHEME IV



Certainly, organolithium reagents also exhibit radical character in many of their reactions,[8-10] thereby making the Gough–Dixon mechanism a likely possibility for their interaction with allylic halides. It should be noted, however, that *cis*- and *trans*-crotyl radicals have been studied by esr techniques which show that they undergo absolutely no interconversion at or below 0° in hydrocarbon solvent.[11]

Thus, all of the suggested mechanisms have invoked an intermediate (ionic or radical) which, by separation from the leaving group,[2,3] bond rotation,[4] or internal return,[5] has forgotten the identity of its precursor to some extent. In direct contrast to these proposals, the reaction of phenyllithium with the parent compound, allyl chloride, gives no evidence requiring the intervention of an intermediate. Allyl chloride, labeled at the α position with either ^2H or ^{14}C, produces allylbenzene, analysis of which shows that the majority of coupling has occurred at the γ position.[12] Clearly, a

$$CH_2{=}CH\overset{*}{C}H_2Cl + PhLi \longrightarrow PhCH_2CH{=}\overset{*}{C}H_2 + CH_2{=}CH\overset{*}{C}H_2Ph$$
$$76\% \qquad 24\%$$

truly symmetrical intermediate (ionic or radical) is not involved here, nor can one account for the product distribution by secondary isotope effects.[12]

In an effort to clarify the mechanistic details of the coupling reaction and to reconcile the allyl chloride results with those that appear to demand an intermediate, we now report on the influence of variously situated methyl substituents on the relative amounts of phenyllithium attack at the α and γ carbons. In the following paper, we describe the stereochemistry of the reaction.

Results

We have investigated the distribution of coupling products from phenyllithium with each of the possible mono- and dimethyl-substituted allylic chlorides (Chart I). Each of these materials is either commercially available or has been reported in the literature. In practice, however, none of these compounds (whether purchased or prepared) was sufficiently pure for use in the coupling reaction. Because of this and the further fact that several of these chlorides tended to decompose and/or isomerize during storage, it was necessary to carefully purify each material (see Experimental Section) and to use it immediately.

Since chlorides **4**, **10**, and **11** are symmetrical in the sense that attack at either the α or γ carbon would yield the same product, it was necessary to distinguish the termini of the allylic system by a suitable isotopic label (Chart II). Monomethyl compound **4**-d_2 was

(6) (a) P. v. R. Schleyer, T. M. Su, M. Saunders, and J. C. Rosenfeld, *J. Amer. Chem. Soc.*, **91**, 5174 (1969); (b) J. M. Bollinger, J. M. Brinich, and G. A. Olah, *ibid.*, **92**, 4025 (1970).

(7) R. G. Gough and J. A. Dixon, *J. Org. Chem.*, **33**, 2148 (1968).

(8) Exchange and coupling reactions with alkyl halides: (a) C. G. Screttas and J. F. Eastham, *J. Amer. Chem. Soc.*, **88**, 5668 (1966); (b) H. R. Ward and R. G. Lawler, *ibid.*, **89**, 5518 (1967); (c) H. R. Ward, R. G. Lawler, and H. Y. Loken, *ibid.*, **90**, 7359 (1968); (d) H. R. Ward, R. G. Lawler, and R. A. Cooper, *ibid.*, **91**, 746 (1969); (e) A. R. Lepley, *ibid.*, **90**, 2710 (1968); *ibid.*, **91**, 749 (1969); *Chem. Commun.*, 64 (1969); (f) A. R. Lepley and R. L. Landau, *J. Amer. Chem. Soc.*, **91**, 748 (1969); (g) G. A. Russell and D. W. Lamson, *ibid.*, **91**, 3967 (1969); (h) F. Gerhart and G. Ostermann, *Tetrahedron Lett.*, 4705 (1969); (i) J. W. Rakshys, Jr., *Chem. Commun.*, 578 (1970).

(9) Additions to multiple bonds: (a) H. R. Ward, *J. Amer. Chem. Soc.*, **89**, 5517 (1967); (b) J. E. Mulvaney, S. Groen, L. J. Carr, Z. G. Gardlund, and S. L. Gardlund, *ibid.*, **91**, 388 (1969); (c) C. Blomberg and H. S. Mosher, *J. Organometal. Chem.*, **13**, 519 (1968); (d) J. K. Crandall and D. J. Keyton, *Tetrahedron Lett.*, 1653 (1969).

(10) Intramolecular rearrangements: (a) F. Gerhart, *ibid.*, 5061 (1969); (b) J. E. Baldwin, J. DeBernadis, and J. E. Patrick, *ibid.*, 353 (1970); (c) E. Grovenstein, Jr., and Y-M. Cheng, *Chem. Commun.*, 101 (1970).

(11) J. K. Kochi and P. J. Krusic, *J. Amer. Chem. Soc.*, **90**, 7157 (1968).

(12) (a) R. M. Magid and J. G. Welch, *ibid.*, **88**, 5681 (1966); (b) R. M. Magid and J. G. Welch, *ibid.*, **90**, 5211 (1968).

CHART I

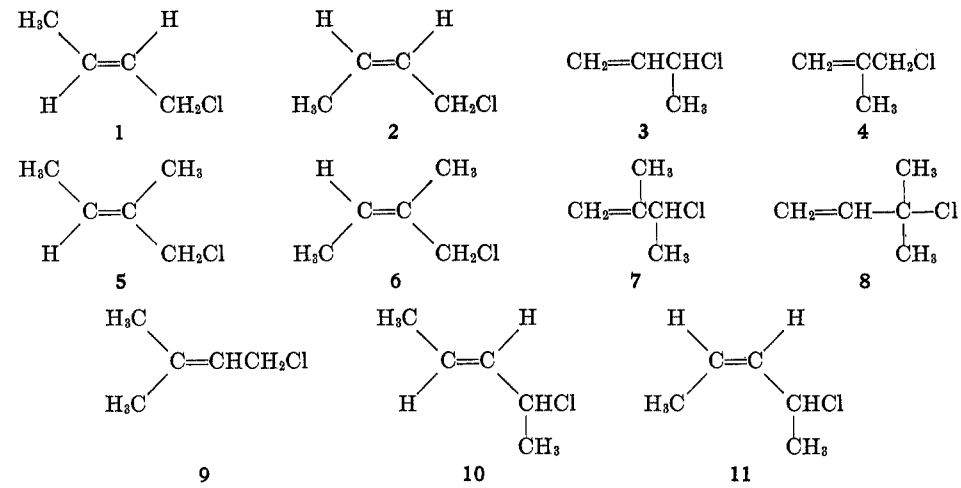
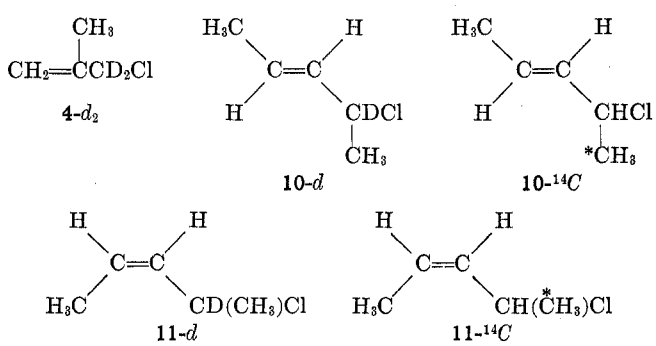
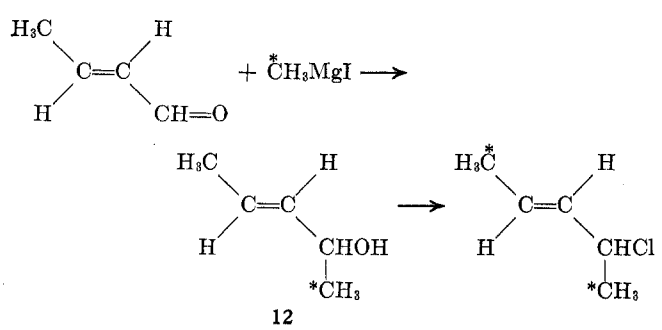


CHART II



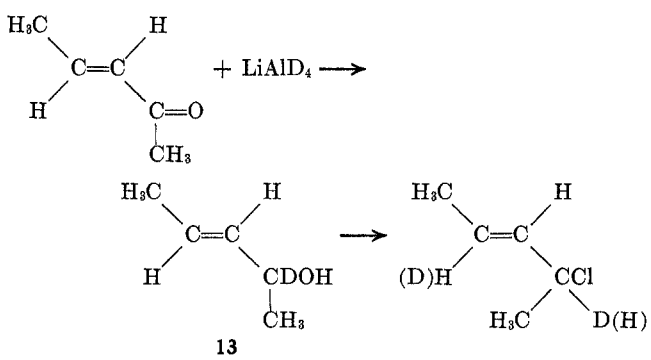
easily prepared by adaptation of established procedures, but enormous difficulties were encountered in the attempted syntheses of ^{2}H- or ^{14}C-labeled **10** and **11**.

A suitable precursor for **10**-^{14}C is alcohol **12** which was prepared by standard methods; degradation of the alcohol confirmed the position of the radioactive carbon. Nearly every attempt to convert **12** into **10**-^{14}C, however, led to complete (or nearly complete)



randomization of the label (see Experimental Section for a compilation of the unsuccessful methods).

The location of the radioactive carbon in **12** and in **10**-^{14}C was determined by ozonolysis[13] and measurement of the activity of the resulting acetaldehyde. Since alcohol **12** was position-specific in its label, we considered the possibility that some or all of the chloride-producing reactions had, in fact, afforded unscrambled **10**-^{14}C and that randomization was occurring during the degradation itself;[15] several reasonably attractive mechanisms for such a process can be imagined. To clarify this point, ^{2}H-labeled alcohol **13** was prepared,



the idea being that one can locate the label in **13** and its derived chloride by nmr analysis both before and after ozonolysis. The numerous failures with radioactive alcohol **12** were once again encountered when **13** was treated with a variety of reagents. Complete or nearly complete scrambling was the general result, the largest label spreads at the α:γ carbons being 57:43 and 65:35 with phosphorous trichloride and phosphorous oxychloride, respectively; in all cases, from 3 to 8% of *cis*-chloride **11** was also produced. It would, therefore, appear that the difficulty resides in the synthesis of the chloride, and, in confirmation of this, ozonolysis of a sample of **10**-*d* having 56% of deuterium at the α carbon and 44% at the γ yielded acetaldehyde which was deuterated to the extent of 44%.

Thus, the method of degradation is reliable, and it must be concluded that none of the alcohol conversions that we tried were very satisfactory. Because of this, the synthesis of the even more labile *cis*-chloride, **11**-*d* or **11**-^{14}C, was not pursued.

The reactions of phenyllithium with monomethyl chloride **3** and dimethyl chlorides **5**, **6**, **7**, **8**, **9**, **10**-*d*, and **10**-^{14}C gave the corresponding coupling product(s) as the only isolable and identifiable materials; in addition to coupling product(s), chlorides **1** and **2** gave small quantities of 1-methyl-2-phenylcyclopropane, and chloride **4** yielded variable amounts of 1-methyl-

(13) This method of degradation was chosen because of its successful application in the analysis of ^{14}C-labeled allyl chloride,[12b,14] and because the conditions can be adjusted to make it milder than other oxidation procedures.

(14) S. H. Sharman, F. F. Caserio, R. F. Nystrom, J. C. Leak, and W. G. Young, *J. Amer. Chem. Soc.*, **80**, 5965 (1958).

(15) This possibility was suggested by Professor W. G. Young, private communication.

TABLE I

YIELDS AND PRODUCT DISTRIBUTIONS IN THE COUPLING OF PHENYLLITHIUM WITH MONO- AND DIMETHYL-SUBSTITUTED ALLYLIC CHLORIDES[a]

	Product yields, %				
	α attack		γ attack		
Allylic chloride[b]	Cis:trans	Total yield	Cis:trans	Total yield	Ratio, α/γ attack
1[c]	0:100	36.3		12.4	74.5/25.5
2[c]	100:0	30.2		9.9	75.3/24.7
3		0.7	17:83	76.2	1.0/99.0
4-d_2		21.7		16.3	57/43
5	0:100[d]	74.8		3.5	95.5/4.5
6	100:0[d]	80.2		6.4	92.6/7.4
7		7.8	30 ± 2:70 ± 2[d,e]	69.8	10.0/90.0
8		Trace		68.2	0/100
9		80.0		Trace	100/0
10-d[f]	g	39.2	g	39.2	50/50
10-d[h]	g	40.0	g	40.0	50/50
10-^{14}C[i]	j	36.6	j	36.6	50/50

[a] The allylic chloride was added to a twofold excess of ethereal phenyllithium at 25°; product yields were determined by quantitative glpc. [b] The isomeric purity of each of the starting materials is given in the Experimental Section. [c] Reference 1a. [d] According to the naming of these compounds as 1-phenyl-2-methyl-2-butenes, the trans compound has the geometry of **5**, and the cis that of **6**. [e] This material was obtained as an inseparable mixture of cis and trans alkenes; the isomer ratio was determined both by nmr peak areas and by glpc (300-ft capillary column, polyphenyl ether). [f] The starting material had 57% deuterium at the α carbon and 43% at the γ and contained 12.5% of the cis isomer. [g] In both cases, the cis:trans alkene ratio was 12:88, but, since neither starting material was free of cis isomer, the mechanistic significance is not clear. [h] The starting material had an α:γ label spread of 65:35 and contained 7% of the cis isomer. [i] The starting material had 58.1% ^{14}C at C_5 and 41.9% at C_1. [j] The cis:trans product ratio was not determined.

cyclopropene.[16,17] The yields and product distributions of the coupling products are summarized in Table I.

With the exception of halides **1**, **2**, and **4**, 70% or more of the starting material was converted into coupling product(s). Competing α elimination with **1**, **2**, and **4** is one reason for the failure to achieve material balance; for the other chlorides, the remainder of material appears to be in the form of unreacted chloride, nondistillable substances (perhaps by elimination of HCl and anionic polymerization of the resulting diene), and high-boiling materials tentatively identified as the coupling products from starting material and biphenyllithium (formed during the preparation of phenyllithium). In no case do we find any C_8 or C_{10} dienes (from Wurtz reaction of the 4- or 5-carbon allylic chlorides), nor are any low-boiling materials (substituted butadienes or dimethylcyclopropenes) produced from the dimethyl compounds.

We can dismiss the possibility that some of the high-boiling materials result from abstraction of the benzylic proton of the hydrocarbon product producing an anion which then couples with starting material.[18] Such a complication would not only lower the overall yield of coupling product but, more seriously, might selectively remove one of the hydrocarbon products from the reaction mixture, thereby making the α/γ attack ratios in Table I unreliable. That this process is not occurring is shown by a number of observations: each of the products from monomethyl compounds **1**–**4** and dimethyl compound **10** can be recovered unchanged when subjected to the reaction conditions; in none of the reaction mixtures are any substituted styrenes found; products having a benzylic deuterium (from chlorides **4**-d_2 and **10**-d) show no loss of the label during the reaction; optically active *cis*- and *trans*-1-phenyl-2-butene-*1*-d containing a full deuterium at the benzylic carbon were obtained from phenyllithium and optically active 3-chloro-*cis*-1-butene-*1*-d.[19] Thus, it is not unreasonable to assume that the lack of material balance is due, exclusively, to processes independent of the coupling reaction. Consequently, the α/γ attack ratios of Table I may be used for meaningful discussion.

Finally, it should be noted that coupling products do not result from an alternate path involving halogen–metal exchange between phenyllithium and allylic chloride followed by coupling of the exchange products;[20] in the systems studied, neither chlorobenzene nor any C_8 or C_{10} dienes are among the reaction products. Products also do not arise by protonation of the allylic anion from phenyllithium addition to butadiene or isoprene, since such reactions give only polymeric materials. For control reactions on the lack of isomerization of the starting allylic chlorides during the reaction, see the Experimental Section.

Discussion

Several features are apparent from inspection of the data of Table I.

1. The product distribution from α-methylallyl chloride (**3**) is distinctly different from that of either *trans*- or *cis*-crotyl chloride (**1** and **2**). Similarly, chloride **7** gives a product ratio different from that of either of its allylic isomers **5** or **6**, although the difference is less pronounced. The only other pair of allylic isomers, **8** and **9**, give the same product, free of its isomer.

2. In those cases involving α attack on pairs of geometric isomers (**1** and **2** or **5** and **6**), the stereochem-

(16) 1-Methyl-2-phenylcyclopropane most likely results from phenyllithium addition across the double bond of 3-methylcyclopropene;[18] α elimination leading to cyclopropene has been conclusively demonstrated to be the first stage in the formation of phenylcyclopropane from allyl chloride and phenyllithium.[12]

(17) Use of halide-free phenyllithium for reaction with chloride **4** provides a highly efficient and convenient synthesis of 1-methylcyclopropene: R. M. Magid, T. C. Clarke, and C. D. Duncan, *J. Org. Chem.*, **36**, 1320 (1971).

(18) Allylbenzene is quantitatively converted by *n*-butyllithium in THF into phenylallyl anion which couples with allyl chloride in high yield: R. M. Magid and S. E. Wilson, unpublished results.

(19) R. M. Magid and E. C. Nieh, *J. Org. Chem.*, **36**, 2105 (1971).

(20) Iodocyclopropanes and methyllithium do couple by such a two-step process: R. M. Magid and S. E. Wilson, *Tetrahedron Lett.*, 4925 (1969).

istry is quantitatively preserved in the product. In cases where γ attack can produce a mixture of geometric isomers, such a mixture does result (**3** and **7**).

3. Introduction of an α-methyl substituent dramatically reduces the α/γ attack ratio (compare allyl chloride[12] with **3**, **4** with **7**, **3** with **8**, **1** with **10**).

4. A γ-methyl group similarly decreases the proportion of reaction at its point of attachment (compare allyl chloride[12] with **1** or **2**, **4** with **5** or **6**, **1** or **2** with **9**, **3** with **10**).

5. A β-methyl substituent tends to increase the α/γ attack ratio, although the effect is less substantial (compare allyl chloride[12] with **4**, **1** with **5**, **2** with **6**, **3** with **7**).

The first of the above features contradicts the observations of Cristol, *et al.*,[3] on the nearly identical product distributions from the reaction of phenyllithium with α-methylallyl chloride (**3**) and crotyl chloride (presumably[12a] a mixture of **1** and **2**). It should be recognized, however, that their separation of products (before the advent of gas chromatography) was accomplished by distillation; consequently, they failed to identify 1-methyl-2-phenylcyclopropane as a product in the crotyl chloride reaction since it most likely codistilled with crotylbenzene.[21] If one adjusts their value of 90–95% crotylbenzene from crotyl chloride by the amount of cyclopropyl compound actually produced, their α/γ attack ratio becomes similar to ours. Thus, one of the criteria for formation of an intermediate may be dismissed. The results with chlorides **5**, **6**, and **7** also do not require a common intermediate nor do our earlier data with labeled allyl chloride.[12] Only chlorides **8** and **9** give the same product distribution (a single compound) and it is possible, although not required, that a change in mechanism to one involving an ionic or radical intermediate has occurred; certainly, the presence of two stabilizing substituents on either the α or γ carbon, could result in such a change. Consistent with this, but once again not demanding it, compound **10** which is substituted at both ends of the allylic system gives equal amounts of α and γ attack.

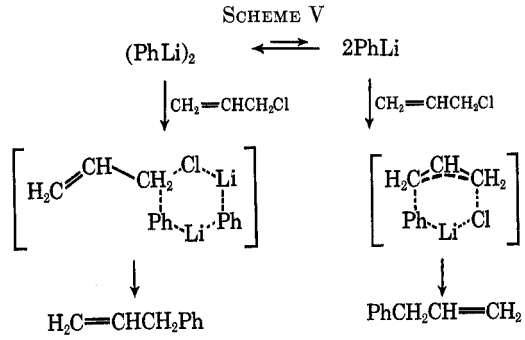
The second feature is in direct conflict with the claim of Wawzonek, *et al.*,[5] that double bond geometry is not preserved in the reactions of phenyllithium with *trans*- and *cis*-crotyl chloride (**1** and **2**). As we have reported earlier,[1a] this apparent loss of stereochemistry is due solely to the use of isomerically impure starting materials. It is significant that even the more highly substituted chlorides **5** and **6** undergo α attack with complete retention of their stereochemical integrity. Thus, another of the criteria for a multistep mechanism must be discarded. One of our principal reasons for investigating the reactions of chlorides **10** and **11** was to ascertain whether substrates bearing substituents that are capable of directly stabilizing an ionic or radical intermediate would still lead to products of retained stereochemistry. Unfortunately, the difficulties in synthesis described earlier prevented our accomplishing this task; the 12% of cis isomer that does result from **10** (Table I, footnote *g*) may merely be due to a combination of γ attack on **10** and α attack on the small amount of cis impurity **11** that is present.

(21) 1-Methyl-2-phenylcyclopropane and *cis*- and *trans*-crotylbenzene are not resolved by a 10-ft, SE-30 glpc column, thus indicating their similar boiling points.

Although all of our data are most simply interpreted without invoking an intermediate, the possibility still exists that ionic or radical[22] species are involved but that they are not so free as to have lost all memory of the structure and stereochemistry of their precursors. One must acknowledge the chance that an intermediate is formed, but that the product-determining transition state is of lower energy than the barriers to significant separation of the leaving group,[2,3] bond rotation,[4] or internal return.[5] The three trends on the influence of α-, β-, and γ-methyl substituents are not especially revealing with regard to drawing mechanistic conclusions, and one can use them in arguing for either concerted or multistep processes.

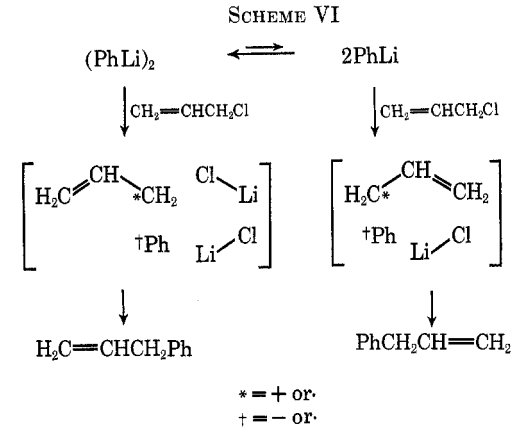
Furthermore, the situation is certainly much more complex than the discussions of other workers would allow. It has been demonstrated that phenyllithium is predominantly dimeric in ether,[23] and the prospect exists that either the monomer or the dimer (or both) is the reactive species in the coupling reaction. One reasonably attractive idea is that α and γ attack are both concerted processes occurring *via* six-membered transition states, the former with dimeric phenyllithium and the latter with monomeric reagent (Scheme V). Kinetic studies should reveal whether the two

SCHEME V



reactions are, indeed, of different kinetic order in phenyllithium, but these have not yet been performed. Should any evidence supporting the idea of an intermediate be found, Scheme V may easily be modified by altering the timing of bondmaking and bondbreaking so that the two transition states are replaced by ionic or radical species (Scheme VI). We prefer to defer

SCHEME VI



(22) Nmr experiments (CIDNP) designed to probe for radical-pair precursors of products gave only negative results: R. M. Magid and F. E. Farrell, unpublished results.

(23) (a) P. West and R. Waack, *J. Amer. Chem. Soc.*, **89**, 4395 (1967); (b) P. West, R. Waack, and J. I. Purmot, *ibid.*, **92**, 840 (1970).

discussion of this point until the following paper in which the stereochemistry of the reaction is described.

Experimental Section

Instruments.—Analytical glpc was performed on a Perkin-Elmer Model 800 gas chromatograph (flame ionization detector) and utilized the following columns: A, 10 ft × 1/8 in., β,β′-oxydipropionitrile (15%) on Chromosorb P; B, a 30 ft × 1/8 in. column composed of a 20-ft section of diethylene glycol succinate (20%) on Chromosorb P (HMDS) and a 10-ft section of Bentone 34 (10%) on Chromosorb P (HMDS); C, 5.5 ft × 1/8 in., Carbowax 20M (20%) on Chromosorb P; D, 20 ft × 1/8 in., Carbowax 20M (10%) on Chromosorb W. In those cases in which quantitative glpc was used for yield determinations, the internal standard method was employed. Peak areas (for yields or product ratios) were measured with a Disc integrator. Preparative glpc was performed on either a Varian Aerograph Model 202-1B gas chromatograph (thermal conductivity detector) or a Hewlett-Packard F & M PrepMaster Jr., Model 776 (flame ionization detector) and utilized the following columns: P, 20 ft × 3/8 in., SE-30 (30%) on Chromosorb P; Q, 10 ft × 3/8 in., SE-30 (20%) on Chromosorb P; R, 8 ft × 1 in., β,β′-oxydipropionitrile (15%) on Chromosorb P; S, 10 ft × 3/8 in., Carbowax 20M (20%) on Chromosorb W; T, 5 ft × 0.25 in., SE-30 (20%) on Chromosorb P; U, 10 ft × 3/8 in., XF-1150 (10%) on Chromosorb P.

Nmr spectra were obtained on a Varian Associates A-56/60A spectrometer. Radioactivity measurements were made with a Packard Tri-Carb Model 3365 liquid scintillation spectrometer. All reactions involving either lithium or organolithium reagents were run in an argon atmosphere.

Materials.—Reagent grade commercial materials were used without further purification, except for the following: thionyl chloride (Matheson Coleman and Bell) was purified by the method of Fieser and Fieser,[24] distilled through a glass helices packed column, and used directly; phosphorus trichloride (J. T. Baker Chemical Co.) was fractionated through a glass helices packed column immediately before use; methyl-^{14}C iodide (50 μCi from Amersham/Searle) was diluted with 500 g of methyl iodide (Matheson Coleman and Bell). Phenyllithium was prepared by the slow addition of bromobenzene in ether to lithium shot[25] in ether at 0–10°, after which the mixture was stored at 0° for 12 hr and filtered through glass wool. By performing this reaction slowly and at relatively low temperature, both the quality and the appearance of the reagent is improved; analysis of the solution was done by the "double titration" method.[26] Halide-free phenyllithium was prepared by the reaction of diphenylmercury and lithium.

Preparation and Purification of Allylic Chlorides.—Each of the starting materials, whether purchased or synthesized, was purified as indicated below and used immediately. The details for 1-chloro-*trans*-2-butene (**1**) and 1-chloro-*cis*-2-butene (**2**) have already been reported.[1a] All of the materials gave spectra consistent with their structures.

A. 3-Chloro-1-butene (3).—Commercial material (Aldrich Chemical Co.) was purified by preparative glpc (column P) and shown to be >99% isomerically pure (column A).

B. 3-Chloro-2-methyl-1-propene-*3,3-d*$_2$ (4-*d*$_2$).—Commercial methacrylic acid was converted into its acid chloride[27] which was reduced by $LiAlD_4$ according to established procedures;[28] the deuterated alcohol was then converted without allylic rearrangement into chloride **4**-d_2 by thionyl chloride and tri-*n*-butylamine in di-*n*-butyl ether.[14] Purification (>99%, column A) was accomplished by preparative glpc (column P); nmr analysis of both the precursor alcohol and chloride **4**-d_2 indicated that the samples were >97% dideuterated at the desired position.

C. 1-Chloro-3-methyl-2-butene (9).—Commercially available material (Eastman) was washed with cold 2% $NaHCO_3$, dried over Drierite, and distilled through a glass helices packed column yielding a substance whose nmr spectrum and glpc analysis (column A) indicated >98% purity.

D. 1-Chloro-2-methyl-*trans*-2-butene (5).—Following the procedure of Young, *et al.*,[29] 3-hydroxy-2-methyl-1-butene was treated in dilute ether solution with thionyl chloride at −50°. Glpc analysis (column A) showed that the crude product was composed of 68% of the desired chloride **5**, 30% of *cis*-chloride **6**, and 2% of allylic isomer **7**. Preparative glpc (column R) yielded material which, by nmr and glpc, was judged to be >97.5% isomerically pure; no improvement in purity could be achieved even after a second preparative glpc.

E. 1-Chloro-2-methyl-*cis*-2-butene (6).—Angelic acid (2-methyl-*cis*-2-butenoic acid) was prepared from butanone in five steps, according to the procedure of Buckles and Mock.[30] Reduction with $LiAlH_4$ yielded 1-hydroxy-2-methyl-*cis*-2-butene which, after fractionation through a glass helices packed column, was judged (nmr and glpc analysis, column D) to be >99% pure. Conversion into chloride **6** was achieved by thionyl chloride and tri-*n*-butylamine in ether at −50°.[29] Flash distillation yielded a material which was >90% chloride **6** (column A); preparative glpc (column R) yielded material which was >99% pure.

F. 3-Chloro-2-methyl-1-butene (7).—Chlorine was bubbled into a solution of 2-methyl-2-butene and 1 equiv of $NaHCO_3$ in ether at 0°.[31] Fractional flash distillation yielded a sample which contained 85% (column A) of the desired chloride; two more flash distillations increased the purity to >98%.

G. 3-Chloro-3-methyl-1-butene (8).—The reaction of gaseous HCl with isoprene in ether at −50°,[32] followed by neutralization with $NaHCO_3$ and distillation through a glass helices packed column [bp 30–32° (120 mm)], yielded material which (nmr and glpc analysis, column A) was >97% pure.

H. 4-Chloro-*trans*-2-pentene-*4-d* (10-*d*).—Reduction of *trans*-2-penten-4-one with $LiAlD_4$ produced the corresponding alcohol **13** which, by nmr analysis, was at least 98% monodeuterated at C-4. Reaction of the alcohol with PCl_3 and pyridine at −40°[33] yielded material which, after two flash distillations, was shown (column D) to be composed of 87.5% trans chloride and 12.5% cis; nmr analysis showed that substantial allylic rearrangement had occurred, 57% of deuterium being at C-4 and 43% at C-2. When $POCl_3$ was substituted for PCl_3 in the above reaction, a somewhat greater label spread was achieved: 65% of deuterium at C-4 and 35% at C-2; 7% of the cis chloride was present.

I. 4-Chloro-*trans*-2-pentene-*5*-^{14}C (10-^{14}C).—The reaction of methyl-^{14}C-magnesium iodide with crotonaldehyde yielded 4-hydroxy-*trans*-2-pentene-*5*-^{14}C (**12**); the position of the label was confirmed by ozonolysis (>99.5% at C_5). Numerous attempts to convert this alcohol into the corresponding chloride while avoiding allylic rearrangement were made, but most of them failed. To summarize, the following reagents led to complete (or nearly complete) scrambling of the label (as determined by ozonolysis): PCl_3 and pyridine in ether at either 0 or −30°; PCl_3 and LiCl in hexamethylphosphoramide at −5°; hexachloroacetone and triphenylphosphine at 15° (modeled after the established procedure with CCl_4 and triphenylphosphine[34] which is unsuitable because of the similar boiling points of CCl_4 and product); thionyl chloride in ether, with or without pyridine (an attempt to prepare the chloride with complete allylic rearrangement[29]). The procedure of Stork, *et al.*,[35] but with methyllithium replaced by pyridine led to extensive elimination.

The best sample of ^{14}C-labeled chloride was obtained by application of the procedure used to prepare ^{2}H-labeled chloride 10-*d* having a 65/35 label spread. From 4.30 g (0.050 mol) of 4-hydroxy-*trans*-2-pentene-*5*-^{14}C (**12**) (2.53 × 10^6 dpm/mol), 7.60 g (0.050 mol) of $POCl_3$, and 1 ml of pyridine was obtained 3.60 g (69%) of labeled chloride, ozonolysis of which produced acetaldehyde whose dimedone derivative had an activity of 1.06 × 10^6 dpm/mol; thus the distribution of ^{14}C in the chloride is 58.1% at C_5, 41.9% at C_1.

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General Procedure for Ozonolysis of Labeled Allylic Alcohols, Allylic Chlorides, and Coupling Products.—The procedure of Young and coworkers[14] for cleavage of allyl chloride was modified to allow milder conditions and to trap acetaldehyde as it was formed. Excess ozone was bubbled through a solution containing *ca.* 0.02 mol of the substrate in 30 ml of methylene chloride maintained at −15°. Solvent was removed with a rotary evaporator (without external heating) and the residue was added to 5 g of zinc dust and 50 ml of 10% aqueous acetic acid at room temperature. Acetaldehyde, thus generated, was swept by a stream of argon (30 ml/min) through an ice–water condenser and into a dimedone trap (*ca.* 300 ml of 0.1 *N* dimedone in sodium acetate–acetic acid buffer, adjusted to pH 5.8).[36] After *ca.* 30 min, the decomposition was complete; the contents of the trap were acidified to pH 4 with acetic acid. Typically, 80% (based upon dimedone) of the 1:2 derivative, mp 140–143°, was formed. Three recrystallizations from methanol–water followed by drying in a vacuum desiccator provided the pure derivative, mp 142–143°.

General Procedure for Reaction of Allylic Chlorides with Phenyllithium.—All reactions were performed by adding a 20% ethereal solution of 0.02–0.10 mol of freshly purified allylic chloride over 15 min to a twofold excess of 0.7–0.8 *N* phenyllithium in ether at room temperature. The reaction mixture was stirred for 2 hr and was hydrolyzed with water. The organic phase was washed with water, dried over Drierite, and concentrated. Quantitative glpc analysis for product yields (ethylbenzene, internal standard) and product distribution were performed on columns B or C for the monomethyl compounds and A or D for the dimethyl. All materials amounting to more than 1% of the total were purified by reduced pressure distillation followed by preparative glpc using columns M or U for the monomethyl compounds and columns S, T, Q, or U for the dimethyl. All products thus isolated were pure (>99%) and their structures were confirmed by nmr analysis and by comparison with authentic samples when available. For reactions in which low-boiling products (methyl-substituted butadienes and cyclopropenes) were anticipated, a stream of argon was swept through the reaction vessel into a Dry Ice–acetone trap whose contents were analyzed by glpc (column D); in every case, the only materials found were ether and unreacted allylic chloride. High-boiling materials (formed in low yield) which would not distil easily at reduced pressure were analyzed by nmr without further purification; they appeared to be mixtures of polymeric material and the coupling products from biphenyllithium and starting material.

Control Reactions.—All of the products were stable to the reaction conditions. In no case was phenyllithium-promoted isomerization to a substituted styrene detected, and alkenes with a benzylic deuterium showed no loss of label. All of the monomethyl allylic chlorides were subjected to the reaction conditions; analysis of aliquots removed at various times showed no isomerization (positional or geometric) and no conversion into allylic bromide (by reaction with LiBr present in phenyllithium). For the monomethyl allylic chlorides, inverse addition of phenyllithium gave no significant change in product yield or distribution nor did the use of halide-free phenyllithium.

Registry No.—**3**, 563-52-0; **4**, 563-47-3; **5**, 23009-73-6; **6**, 23009-74-7; **7**, 5166-35-8; **8**, 2190-48-9; **9**, 503-60-6; **10**, 18610-33-8; phenyllithium, 591-51-5.

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The Coupling Reaction of Phenyllithium with Allylic Chlorides. The Stereochemistry of the Reaction[1a]

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The stereochemistry of γ coupling of phenyllithium with optically active 3-chloro-*cis*-1-butene-*1-d* has been determined. The results are interpreted in terms of a mechanism (concerted or stepwise) which proceeds greater than 95% by attack of phenyllithium syn to the leaving group.

In the preceding paper,[2] several mechanisms for the coupling of allylic chlorides with phenyllithium were discussed. Product and geometric isomer data from the reactions of mono- and dimethyl-substituted allylic chlorides led to the conclusion that the coupling at both the α and γ carbons either is a direct one-step process or involves intermediates (ionic or radical) which are separated from products by a relatively low energy barrier (*i.e.*, their lifetimes are not long enough to allow loss of memory of the structure and geometry of their precursors). In this paper, we report on the stereochemistry of the coupling reaction with optically active allylic chlorides.

Results

In order to fully elucidate the stereochemistry of the coupling reaction, a substrate which meets all of the following conditions is required.

1. It must have an asymmetric α-carbon atom. 2. Two different substituents must be present on the γ carbon, and the geometry of the double bond must be well defined. 3. Coupling reaction should occur at both allylic positions, and the α- and γ-coupling products must be cleanly separable, one from the other. 4. γ attack must produce a *separable* mixture of cis and trans olefins. 5. The absolute configuration and maximum rotation of the allylic chloride and of its coupling products should be able to be determined with a reasonable degree of accuracy.

The reaction of phenyllithium with a substrate (of generalized structure **1**) meeting all of these conditions is illustrated in Scheme I.[3] Our initial plan was to use optically active 4-chloro-*trans*-2-pentene (**1**, $R_1 = R_4 = CH_3$; $R_2 = R_3 = R_5 = H$), unsymmetrically labeled with either ^2H or ^{14}C. Unfortunately, we were unable to prepare this material with a sufficiently large label spread and with clearly defined double bond geometry.[2] Furthermore, we were doubtful of the likelihood of obtaining this substance in an optically stable form in view

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