The Generation of Allyllithium Reagents by Lithium–Tetrahydrofuran Reduction of Allylic Mesitoates. A New Procedure for Selective Allylic Cross Coupling and Allylcarbinol Synthesis

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A variety of allylic mesitoates undergo alkyl–oxygen fission upon reduction by lithium metal in tetrahydrofuran at 0°. The allylic organolithium thus generated is sufficiently stable to undergo reactions with electrophilic species present *in situ*. *In situ* reaction with allylic bromides produces fair to excellent yields of 1,5-dienes in a cross-coupling reaction that is considerably more selective than Wurtz-type procedures, in regard to crossed nature and retention of double bond position and geometry. *In situ* reaction with aldehydes and ketones gives moderate to good yields of allylic carbinols, and has been used to synthesize a component of the *Ips confusus* pheromone. Both reactions are convenient and possess certain advantages over other currently available methods.

The allylic unit is a common structural feature of many compounds of natural origin and theoretical interest. One of the simplest synthons for such units is the allylic organometallic; however, the synthetic utility of allylic organometallics is seriously hampered by problems associated with their generation and ambiguities inherent in their pattern of reactivity. Coupling is often a major side reaction in the preparation of these reagents,[1] and reaction with electrophiles generally gives products consisting of mixtures of allylically transposed and geometrically isomerized materials.[2]

As part of a study of new approaches to the stereoselective synthesis of olefinic systems, we considered the possibility of generating an allylic organometallic reagent *in situ* in the presence of an electrophilic counterpart. Such an approach would minimize the lifetime of the allylic anion and might thus avoid some of the operational problems mentioned above. In particular, we sought to reduce the extent of cis-trans isomerization in some of the more highly substituted allylic anions and to avoid production of undesired self-coupling products.

The following three criteria must be met by the components of the *in situ* reaction scheme proposed above: (1) the precursor of the allylic organometallic must be inert toward attack by the allylic anion being generated (at least relative to the electrophile, with which reaction is desired); (2) the electrophile must survive, unaltered, the conditions necessary to generate the allylic anion from its precursor; and (3) the solvent must be compatible (at least for a short time period) with the allylic organometallic.

We have recently reported that a variety of allylic organometallic reagents can be generated, albeit transiently, by the action of lithium metal in tetrahydrofuran on allylic mesitoate esters,[3,4] and we have shown that this process can function in an *in situ* manner with allylic halides as the electrophilic species to produce 1,5-dienes (Scheme I).[3] This report provides a detailed description of the allyllithium generating system, and presents further results on the *in situ* 1,5-diene synthesis. In

addition, it describes the extension of the lithium–allyl mesitoate method to the synthesis of allylic carbinols in a second *in situ* process, utilizing aldehydes and ketones as electrophiles (Scheme IV).

Results and Discussion

A. The Allylic Organolithium Generating System. — Allyllithium species are presumed to be the intermediates in a number of reductive alkyl–oxygen fission reactions of allylic and benzylic alcohol derivatives.[5,6] Most notable of these, the Henbest reduction of allylic benzoates with lithium in ethylamine,[7] has been of considerable synthetic utility as a deoxygenation procedure. There have been no reports, however, of the interception of the allylic anion by an electrophilic species; indeed, it is doubtful that the carbanion even has an appreciable lifetime before it undergoes protonation by the amine solvent. Nevertheless, it did seem likely that, with appropriate modification, the Henbest procedure might provide a method of generating allylic organometallics that would be suitable for use in a reaction with electrophiles present *in situ*.

Our selection of the mesitoate ester–lithium in tetrahydrofuran combination resulted from the following considerations. It is clear that the solvent must be aprotic for the organometallic to survive even briefly (criterion 3). As Eisch[8] and others[9] have reported the generation of allyllithium by reduction of allyl phenyl ether with lithium in tetrahydrofuran, these seemed to be resonable choices for reducing agent and solvent. The mesitoate ester was selected in preference to the benzoate for reasons related to the demands of criterion 1. The well-known reluctance of mesitoate esters to undergo nucleophilic addition at the acyl center[10] should make them considerably more inert than the benzoates toward attack by the allyllithium species

(1) H. Gilman and J. H. McGlumphy, *Bull. Soc. Chim. Fr.*, **43**, 1323 (1928).

(2) R. A. Benkeser, *Synthesis*, 347 (1971).

(3) J. A. Katzenellenbogen and R. S. Lenox, *Tetrahedron Lett.*, 1471 (1972).

(4) For a related study involving reductive cleavage of cyclopropylcarbinyl mesitoates, see J. A. Katzenellenbogen and T. Utawanit, *ibid.*, 1475 (1972).

(5) M. Smith in "Reduction," R. L. Augustine, Ed., Marcel Dekker, New York, N. Y., 1968, Chapter 2.

(6) Evidence for the intermediacy of the allylic anion comes from the fact that double bond isomerization often accompanies these reductions. Furthermore, the rate-retarding effect observed with increased alkyl substitution on the carbinol carbon is more consistent with anionic species than with radicals. See A. J. Birch, *J. Chem. Soc.*, 809 (1945); A. J. Birch, *Quart. Rev., Chem. Soc.*, **4**, 69 (1950).

(7) A. S. Hallsworth, H. B. Henbest, and T. I. Wrigley, *J. Chem. Soc.*, 1969 (1957).

(8) J. J. Eisch and A. M. Jacobs, *J. Org. Chem.*, **28**, 2145 (1963).

(9) P. Miginiac and C. Bouchoule, *Bull. Soc. Chim. Fr.*, 4156 (1968).

(10) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1959, p 325.

being generated. The compatability of various electrophiles with lithium in tetrahydrofuran was the only aspect of the *in situ* process (criterion 2) that lacked adequate precedent.

Mesitoate esters of allylic alcohols can be prepared conveniently and in high yield by a slight modification of the procedure of Higgins,[11] utilizing mesitoyl chloride in pyridine–chloroform. They are easily purified and show no tendency to undergo cis–trans isomerization or allylic transposition either during their preparation or after prolonged storage at room temperature.

To investigate the efficiency of the allylic organolithium generating process and the stability of the mesitoate precursor toward the organometallic being generated, allyl mesitoate alone was treated with lithium in tetrahydrofuran. Within minutes at 0° the reaction turned deep red; the production of allyllithium was monitored periodically by gas evolution; and the titer as a function of time is illustrated in Figure 1.

Although the allyl mesitoate is completely consumed within 1.5 hr under these conditions, at no time does the allyllithium titer exceed 12% of the theoretical yield. Further investigation (*vide infra*) has established that, in the absence of added electrophiles, the allyllithium is consumed primarily by reaction with its precursor, allyl mesitoate.

This experiment indicates the extent to which the lithium–allyl mesitoate generating system satisfies criterion 1. However, as will be shown subsequently, when electrophiles are present (in the *in situ* reactions), they can compete quite efficiently for reaction with the allyllithium species, so that its reaction with starting material can become insignificant.

B. Allylic Coupling.—Despite its semblance of simplicity, the synthesis of 1,5-dienes by the direct coupling of allylic species is an approach that suffers from severe experimental limitations. Both the Grignard and Wurtz-type couplings result in complex mixtures of symmetrical and unsymmetrical products which show loss of double-bond geometry and position in at least one of the allylic units.[12]

Two more recent methods, one employing the coupling of π-allylnickel(I) halide complexes with allylic bromides[13] and the other a titanium-promoted deoxygenative coupling of allyl alcohols,[14] also suffer from a lack of efficient cross coupling, showing almost statistical mixtures of coupled products when two different allylic units are used. Two other methods, based on sulfur-[15] and phosphorus-stabilized[16] allylic anions, appear to give efficient cross coupling, but require a subsequent step to remove the stabilizing substituent. Allyl and methallyl Grignard have been efficiently cross coupled with allylic chlorides, but the stereochemical fate of the Grignard-derived portion of the molecule cannot be determined in these systems.[17]

(11) G. M. C. Higgins, B. Saville, and M. B. Evans, *J. Chem. Soc.*, 702 (1965).
(12) D. Barnard and L. Batemann, *ibid.*, 932 (1950).
(13) E. J. Corey, M. F. Semmelhack, and L. S. Hegedus, *J. Amer. Chem. Soc.*, **90**, 2416 (1968).
(14) E. E. van Tamelen, B. Akermark, and K. B. Sharpless, *ibid.*, **91**, 1552 (1969), and references cited therein.
(15) J. F. Bielmann and J. B. Ducep, *Tetrahedron Lett.*, 3707 (1969).
(16) E. H. Axelrod, G. M. Milne, and E. E. van Tamelen, *J. Amer. Chem. Soc.*, **92**, 2139 (1970).
(17) (a) G. Stork, P. A. Grieco, and M. Gregson, *Tetrahedron Lett.*, 1393 (1969). (b) P. A. Grieco, *J. Amer. Chem. Soc.*, **91**, 5660 (1969).
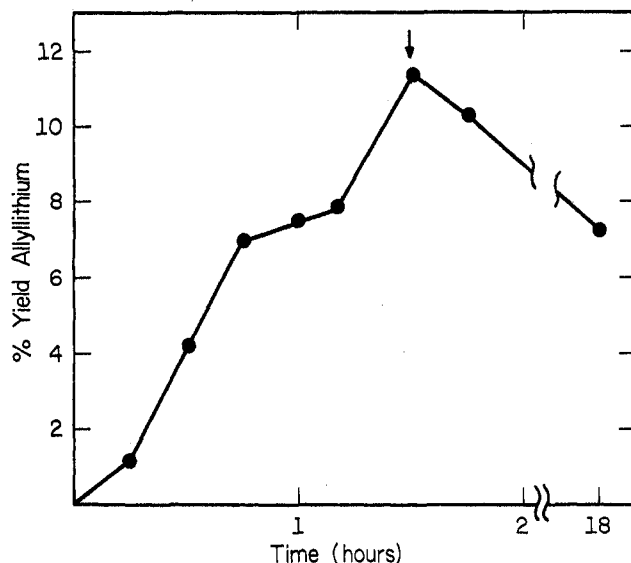

Figure 1.—Titer of allyllithium generated by reaction of allyl mesitoate with lithium in tetrahydrofuran. Arrow indicates the time at which allyl mesitoate consumption was complete.

1. Synthesis of 1,5-Dienes. Lithium Reduction of Allylic Mesitoates with Allylic Bromides *in Situ*.—As we have recently reported,[3] 1,5-dienes can be synthesized in a selective cross-coupling reaction by generating an allylic organolithium reagent according to the mesitoate–lithium procedure with an equimolar amount of allylic bromide present *in situ* as the electrophile (Scheme I). The reaction mixture in this case remains clear and colorless for ca. 0.5–1 hr at 0°, turning to a characteristic deep red within a matter of seconds as soon as the bromide has been consumed. Maximum yields are obtained if the reaction is quenched at this point. The results of our study of this reaction are summarized in Table I.

SCHEME I
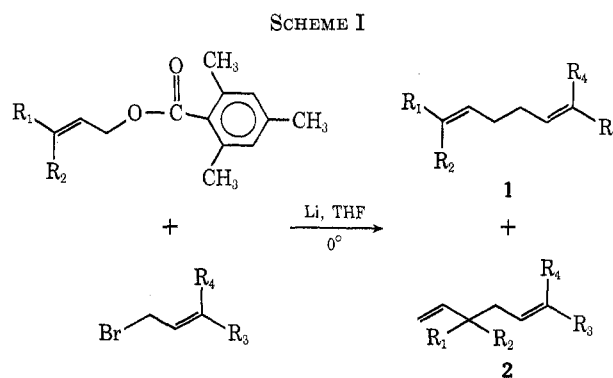
1,2	R₁	R₂
a	$(CH_3)_2C{=}CH(CH_2)_2$	CH_3
b	$(CH_3)_2C{=}CH(CH_2)_2$	CH_3
c	$(CH_3)_2C{=}CH(CH_2)_2$	CH_3
d	$(CH_3)_2C{=}CH(CH_2)_2$	CH_3
e	CH_3	CH_3
f	CH_3	H
g	H	H

1,2	R₃	R₄
a	H	H
b	CH_3	CH_3
c	$(CH_3)_2C{=}CH(CH_2)_2$	CH_3
d	$(CH_3)_2C{=}CH(CH_2)_2(CH_3)C{=}CH(CH_2)_2$	CH_3
e	$(CH_3)_2C{=}CH(CH_2)_2$	CH_3
f	$(CH_3)_2C{=}CH(CH_2)_2$	CH_3
g	$(CH_3)_2C{=}CH(CH_2)_2$	CH_3

TABLE I

PRODUCTS AND YIELDS OF CROSS COUPLING REACTIONS

	Mesitoate	Bromide	% yield[a] dienes	Isomer ratio	% Mesitoic acid recovered
1	Geranyl	Allyl	60 (35)	1a (80):2a (20)	66
2	Geranyl	3-Methyl-2-butenyl	(49)	1b (72):2b (18)	73
3	Geranyl	Geranyl	95 (93)	1c (60):2c (40)	61
4	Geranyl	Farnesyl	43	1d (77):2d (23)	
5	3-Methyl-2-butenyl	Geranyl	32	1e (65):2e (35)	43
6	trans-2-Butenyl	Geranyl	19	1f (55):2f (45)	11
7	Allyl	Geranyl	22	1g (100)	37

[a] Yields determined by glpc using internal standards. Yields given in parentheses are isolated yields.

The overall yield of coupling product by this process is quite variable, but appears to be highest when the allylic fragment derived from the mesitoate is more highly substituted (1–4 *vs.* 6 and 7). From the high yield in certain select cases (3) it is clear that all three criteria, as outlined in the first section, can be adequately met. However, it was of interest to determine whether the electrophilic component would be stable under the reaction conditions.

In separate experiments, geranyl, farnesyl, 3-methyl-2-butenyl, and allyl bromides were treated with lithium under conditions identical with those of the coupling reaction. The lower molecular weight bromides were found to undergo a rather rapid Wurtz coupling, thus giving high yields of self-coupled products in the time periods used for coupling by the mesitoate lithium procedure. Geranyl and farnesyl bromides showed some coupling, but the rate of this self-coupling process was much slower than the cross-coupling reaction.

The implication of these experiments is that certain allylic bromides, namely those of lower molecular weight, may be relatively unstable under the reaction conditions. In these cases reduced yields of cross-coupled products in the mesitoate–lithium procedure may be attributed in part to consumption of the electrophile, while reduced yields using higher molecular weight bromides may result from nonproductive consumption of both the electrophile and the allyllithium precursor (*vide infra*).

The products of the coupling reaction are mixtures of direct and transposed types with allylic transposition being limited to the allylic portion derived from the mesitoate. This can be seen by comparing the two allyl–geranyl couplings (1 and 7). The reaction of allyl mesitoate with geranyl bromide (entry 7) gives only one diene product, as allylic transposition in the nucleophile leads to the same product as direct coupling without rearrangement; however, the reaction of geranyl mesitoate with allyl bromide (1) gives two diene products, the minor one arising from allylic transposition of the geranyllithium species. These results are consistent with the known ambient behavior of allylic anions in coupling reactions.[2] No evidence of products arising from SN2' attack on the bromide has ever been found in the mesitoate–lithium coupling reaction, al-

though this side reaction has been observed on many occasions in allylic coupling reactions.[11,17a,18]

The fact that only the mesitoate-derived portion of the 1,5-diene is subject to transposition in the unsymmetrical couplings (3–8) substantiates the fact that the nucleophilic fragment is derived from the mesitoate, and not the bromide. However, there are several reports in which allyl mesitoates and other hindered allyl esters have served as electrophiles in coupling reactions with alkyl and benzyl Grignard reagents.[11,19] Although reactions were run in the absence of free metal, using refluxing ethyl ether as a solvent (conditions under which our coupling reaction fails to work), we felt that it was important to establish unequivocally that the mesitoate is acting only as a source of nucleophile, and that no 1,5-diene is produced from the reaction of allyl bromide derived allyllithium with the mesitoate. Geranyllithium, generated from its phenyl ether,[8] was allowed to react with allyl mesitoate; no cross-coupling products could be detected. The small amount of geranyl dimer observed was produced during the geranyllithium preparation[9] and was present prior to the attempted couplings. In a separate experiment it was shown that no coupling product (digeranyl) was formed when geranyl mesitoate alone was treated with lithium in tetrahydrofuran.

A factor of prime importance in assessing the efficiency of an allylic coupling reaction is the degree of cross coupling that can be achieved. The advantage of the *in situ* mesitoate procedure over a Wurtz-type procedure in this regard is evident from the data presented in Table II. A geranyl–farnesyl coupling was

TABLE II

COUPLING OF GERANYL AND FARNESYL UNITS

Reactants	Yield of C_{25} products, %[a]	Relative ratios, %[b]		
		Ger–Ger[c] C_{20}	Ger–Far C_{25}	Far–Far C_{30}
trans-Geranyl bromide, trans,trans-farnesyl bromide, magnesium	32	13	30	57
trans-Geranyl mesitoate, trans,trans-farnesyl, bromide, lithium	43	14	62	24

[a] Determined by glpc using internal standards. [b] Glpc area ratio corrected for molecular weight differences. [c] Ger = geranyl; Far = farnesyl.

performed by reaction of the respective bromides with magnesium in ether at reflux and by the *in situ* method using geranyl mesitoate and farnesyl bromide. The proportion of product that is cross coupled is twofold greater in the mesitoate procedure than in the magnesium one; the overall yield of the former process is greater as well.

Since we have shown that Wurtz-type coupling of mesitoates alone does not take place under the conditions of the 1,5-diene synthesis, the C_{20} product (geranyl dimers, Ger–Ger) must result from a metal–halogen

(18) It has been reported (ref 11) that selective hydroboration using disiamylborane can reduce the fraction of transposed (vinyl-containing) product in a coupling mixture to less than 2%.
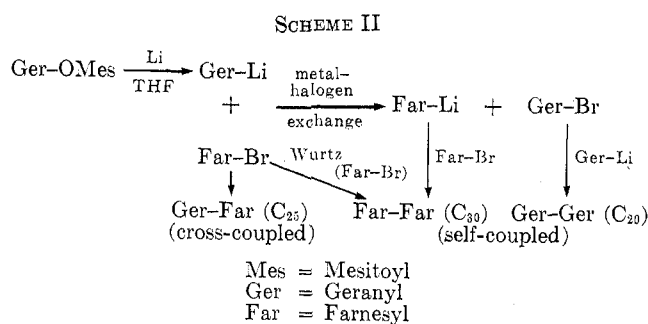
(19) R. T. Arnold and R. W. Liggett, *J. Amer. Chem. Soc.*, **64**, 2875 (1942); R. T. Arnold and R. W. Liggett, *ibid.*, **67**, 337 (1945); E. J. Corey, S. W. Chow, and R. A. Scherrer, *ibid.*, **79**, 5773 (1957).

TABLE III

PRODUCT DISTRIBUTIONS FROM GERANYL–NERYL COUPLINGS

| | Mesitoate | Bromide | Relative yield, $\%^a$ | | | | | Total^b yield, % | Yield of mesitoic acid, % |
			1c	2c	3	4	5		
1	Geranyl	Geranyl	*77*^{c}	*23*	0	Trace^d	Trace	95	31
2	Neryl	Neryl	trace	9	59	13	*19*	95	10
3	Geranyl	Neryl	11	15	10	*54*	10	95	13
4	Neryl	Geranyl	16	*16*	13	*45*	10	95	6

^{a} Determined by glpc; area ratios. ^{b} Determined by glpc using internal standards. ^{c} Expected coupling products are italicized. ^{d} Trace is <2%.

exchange reaction followed by a self-coupling (Scheme II). An equal amount of C_{30} product (farnesyl dimer,

SCHEME II

Ger–OMes $\xrightarrow[\text{THF}]{\text{Li}}$ Ger–Li $\xrightarrow[\text{exchange}]{\text{metal-halogen}}$ Far–Li + Ger–Br

Mes = Mesitoyl
Ger = Geranyl
Far = Farnesyl

Far–Far) could also arise as a result of this exchange. A portion of the C_{30} product may also arise from a direct self-coupling (Wurtz) of the farnesyl bromide.

Further examination of the glpc traces of the products produced in the experiments described in Table II revealed two additional advantages of the mesitoate coupling procedure over the Wurtz-type method. The C_{25} product from the mesitoate procedure has suffered noticeably less allylic transposition (20%) than that from the Grignard procedure (30%), and the per cent cis double bond found in the nontransposed C_{25} product was also less in the mesitoate procedure (5%) than in the Grignard procedure (10%).

As one of the motivations for devising an *in situ* allylic cross-coupling procedure was our desire to reduce the extent of cis–trans isomerization that occurs in the allylic anion, this question was pursued in greater detail. Table III contains data describing the distribution of products (Scheme III) from four cross-

SCHEME III

1c

2c

3

5

4
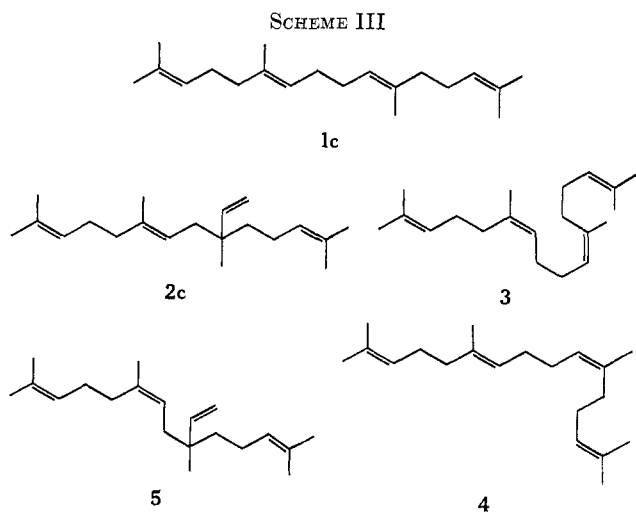
coupling reactions utilizing all possible combinations of neryl and geranyl units. The overall yields of these couplings are high, consistent with the structure–yield correlations discussed in relation to Table I. It is evident, however, that cis–trans isomerization is taking place in some cases (entries 2–4). The geometric purity of the products from the geranyl–geranyl coupling (entry 1), however, indicates that at least in this instance geometric isomerization (trans to cis) can be kept to a minimum. The presence of geometrically isomerized products (2c and 4) in the neryl–neryl coupling (entry 2) establishes that some cis to trans isomerization is occurring; the difference between these two coupling experiments may represent the greater stability of the trans isomer of the allyllithium species of

trans ⇌ cis
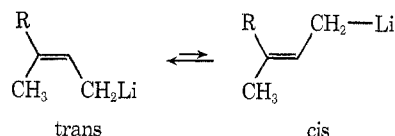
this particular substitution pattern. The other two entries in Table III represent cross coupling between neryl and geranyl units. Here a considerable proportion of the products appear to be geometrically isomerized. However, many of the isomers could only be produced subsequent to a metal–halogen exchange (*e.g.*, entry 4, product 3: neryllithium + geranyl bromide → neryl bromide + geranyllithium; then neryl bromide + neryllithium → 3) or by Wurtz coupling of the electrophile. It is difficult to factor out the per cent cis–trans isomerization that has taken place in these cases.

We have been unsuccessful in extending this coupling reaction to nonallylic systems. No coupling is observed when a primary alkyl group is substituted for allyl in either the mesitoate or the bromide. Furthermore, no coupling is detectable if an allylic benzoate is used in place of the corresponding mesitoate. Inclusion of biphenyl or dimethyl sulfoxide in the tetrahydrofuran solvent did not affect the yield or stereoselectivity of the coupling; with hexamethylphosphoramide as cosolvent, yields were decreased.

2. Side Reactions Accompanying the 1,5-Diene Synthesis.—Mesitoic acid can be recovered from these coupling reactions by sodium hydroxide extraction of the reaction mixture. The per cent recovery from a number of reactions are found in Tables I and III. It is evident that the yield of recovered acid varies widely, indicating that the mesitoate portion is being consumed through some secondary process. Indeed, treatment of mesitoic acid alone with lithium in tetrahydrofuran resulted in the generation of the deep red-brown color observed in the coupling reactions them-

selves. A methyl iodide quench of this reaction mixture allowed the isolation of a number of reduction products, two of which were tentatively identified by spectroscopic means as the benzyl methyl ethers **6** and **7**;[20] the structure of **6** was confirmed by an independent synthesis.

To investigate further the extent to which the mesitoate group is reduced, allyl mesitoate was similarly reduced and methylated. Glpc–mass spectroscopic analysis of the products obtained after quenching the dark red solution with methyl iodide showed at least 13 products ranging in molecular weight from 134 to 246. One of these products was shown by its mass spectrum to be 2,4,6-trimethylethylbenzene (**8**); no structures have been assigned to the remaining compounds.
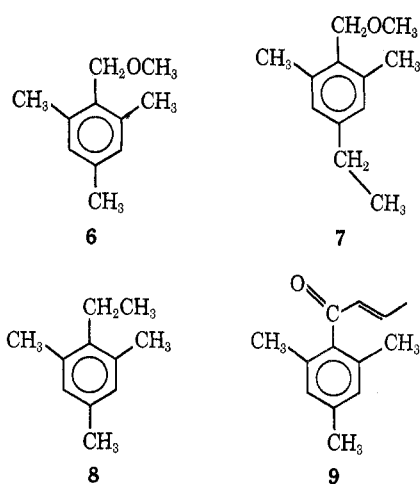

The unsaturated ketone **9** has been found as a byproduct in a number of the coupling reactions utilizing allyl mesitoate. It results from allyllithium attack on allyl mesitoate, the double bond shifting into conjugation during the normal aqueous acid work-up. Indeed, **9** can be synthesized in 65% yield by the reaction of allyl mesitoate with allyllithium prepared from allyl phenyl ether.[8] Production of **9**, and presumably analogous ketones in other coupling reactions, reduces the yield of the desired product by consuming both the allyllithium and the allyllithium precursor.

C. Carbonyl Additions.—The synthesis of allylic carbinols from carbonyl compounds and allylic nucleophiles has been carried out in many different ways. The addition of a preformed allylic Grignard reagent to a carbonyl compound is often not a desirable method for two reasons. It requires the synthesis of the necessary allylic halide, and subsequently, generation of the allylic Grignard reagent, a step which can lead to extensive allylic coupling.[1] A recent communication has described the synthesis of carbinols by the reaction of a carbonyl compound and an organohalide together with lithium in tetrahydrofuran.[21] This *in situ*, Reformatsky-type procedure has been reported several times for the specific cases of allylic and propargylic halides using magnesium,[22] zinc,[23] or aluminum[24] as the reduc-

(20) Spectroscopic evidence does not allow distinction between structure **9** and the isomer with the ethyl ortho to the methoxymethyl substituent.

(21) P. J. Pearce, D. H. Richards, and N. F. Scilly, *Chem. Commun.*, 1160 (1970).

(22) M. P. Dreyfuss, *J. Org. Chem.*, **28**, 3269 (1963).

(23) M. Gaudemar, "Les Derives Organo-Metalliques," Colloques Internationaux du Centre National de la Recherche Scientifique, No. 120, Paris, 1963, p 133.

(24) M. Gaudemar, *Ann. Chim. (Paris)*, **1**, 161 (1956).

ing agent. The use of magnesium in this manner has been termed the Barbier–Grignard reaction, and, although known for many years, the reaction fell into disuse until 1963.[22]

We have found that the *in situ* generation of allyl organolithium reagents can also be used to produce allylic carbinols, using aldehydes and ketones as electrophiles *in situ*. Although this method gives somewhat lower yields when compared to the zinc and magnesium methods mentioned above, it avoids the necessity of synthesizing an allylic halide. Also, side reactions such as α-alkylation of the carbonyl compound are minimized. Such side reactions often accompany the synthesis of carbinols by the Barbier–Grignard reaction and make the separation and purification of the carbinol extremely difficult in many instances. In cases where the carbonyl compound prossesses no α hydrogens, the use of allylic mesitoates appears to be the method of choice for carbinol formation.

1. Synthesis of Allyl Carbinols. Lithium Reduction of Allylic Mesitoates with Aldehydes and Ketones *in Situ*.—Treatment of an allylic mesitoate (**10**) and an aldehyde or ketone (**11**) in equimolar amounts with lithium under the same conditions used to produce 1,5-dienes results in rapid formation of the desired allylic carbinol (**12**) (Scheme IV) whch may be readily isolated

SCHEME IV
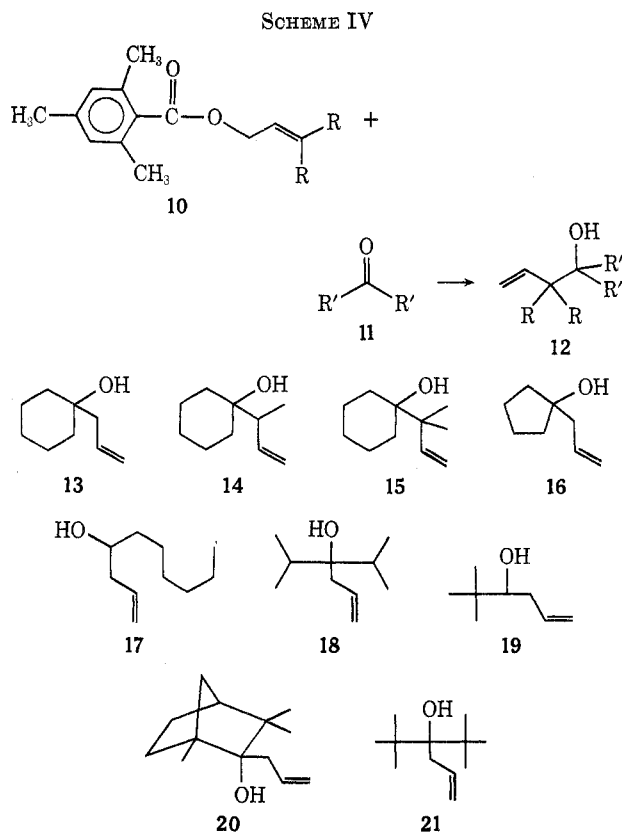
by distillation or chomatography. As is the case with the magnesium and zinc procedures, the product has the allylic group attached at the more highly substituted terminus, regardless of the point of attachment of the mesitoate group in the starting ester. Table IV compares the results of the mesitoate method applied to several model systems with the magnesium and zinc procedures.

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TABLE IV

SYNTHESIS OF ALLYLIC CARBINOLS

</div>

	Carbinol	Allylic component	Carbonyl compound	Yield, %,[a] mesitoate procedure	Yield, %,[b] "Reformatsky" procedure	Metal used
1	13	Allyl	Cyclohexanone	42 56[c]	95	Mg
2	14	2-Butenyl	Cyclohexanone	39	72	Zn
3	14	1-Buten-3-yl	Cyclohexanone	35		
4	15	3-Methyl-2-butenyl	Cyclohexanone	22	64	Zn
5	15	3-Methyl-1-buten-3-yl	Cyclohexanone	25		
6	16	Allyl	Cyclopentanone	27	80	Mg
7	17	Allyl	Heptanal	14	69	Zn
8	18	Allyl	Diisopropyl ketone	60	75[d]	Mg
9	19	Allyl	Pivaldehyde	64 (49)	84	Zn
10	20	Allyl	Fenchone	67	50	Mg
11	21	Allyl	Di-t-butyl ketone	54, 52	75	Mg

[a] Determined by glpc using standards. Isolated yields in parentheses. [b] All yields from Reformatsky procedures are isolated yields. [c] Using 2 equiv of allyl mesitoate. [d] Allylmagnesium bromide used directly as Barbier–Grignard was unsatisfactory.

In most cases, the yield by the mesitoate lithium procedure is considerably lower than that of the Reformatsky-type procedures. However, it is notable that, in those cases in which the carbonyl component is severely hindered (entry 8) or has no α hydrogens (entries 9,10,11), the yield of alcohol by the mesitoate procedure is competitive or even superior to that of the Reformatsky procedure. Also, reaction conditions have not been optimized; the use of 2 equiv of allyl mesitoate improved the yield in the one case investigated (entry 1).

To demonstrate further the utility of the mesitoate reaction, we have synthesized one of the sex attractants (24) of *Ips confusus*, a bark beetle common to Ponderosa pine, by the mesitoate procedure and for comparison by the zinc method, using isovaleraldehyde (22) and 2-bromomethyl-1,3-butadiene (23a). Previously, it has been reported that the classical Grignard alcohol synthesis could not be utilized because the Grignard reagent of 2-bromomethyl-1,3-butadiene (23a) could not be prepared; in this case, the attractant was prepared by a several-step synthesis involving reaction between the anion of 2-isobutyl-1,3-dithiane and the bromide 23a[25]

Our results with both the mesitoate–lithium and zinc procedures demonstrate that the direct alcohol synthesis is a possible route to this attractant. The reaction of 2-(mesitoyloxymethyl)-1,3-butadiene (23b) with lithium in tetrahydrofuran in the presence of isovaleraldehyde (22) gave a 10% isolated yield of the attractant 24. The ester 23b was prepared from the corresponding alcohol, which was made by a modification of a procedure given by Thomas.[26] Similarly, 23a

(25) C. A. Reece, J. O. Rodin, R. G. Brownlee, W. G. Duncan, and R. M. Silverstein, *Tetrahedron*, **24**, 4249 (1968).
(26) A. F. Thomas, *J. Amer. Chem. Soc.*, **91**, 3281 (1969).

reacts readily with zinc in the presence of isovaleraldehyde in refluxing tetrahydrofuran to give the attractant in 52% yield after purification.

2. Side Reactions Accompanying Carbinol Formation.—Side reactions in the formation of allylic carbinols seem to be less complex and troublesome than those encountered in the allylic couplings. Examination of reaction mixtures by glpc frequently indicated that even when the mesitoate was consumed, considerable starting ketone or aldehyde could be detected. As the reactions were quenched by the addition of water, the presence of aldehyde or ketone suggested that α-hydrogen abstraction from the carbonyl compound by the generated allyllithium was a significant side reaction. Accordingly, allyl mesitoate was treated with cyclohexanone under the conditions used to give the yields shown in Table IV, and the reaction mixture was quenched with allyl bromide. 2-Allylcyclohexanone was found to be present along with the desired carbinol 13. The high yields obtained by our method using carbonyl compounds containing no α hydrogens further substantiate the abstraction of hydrogen as an important side reaction. None of ketone 9 could be detected in reactions employing allyl mesitoate.

<div style="text-align:center">

Experimental Section

</div>

Tetrahydrofuran (THF) was dried by distillation from sodium naphthalide and was used immediately. Ethanol-free chloroform was prepared by passing reagent chloroform (Fisher) through a column of alumina (Merck, neutral). Lithium wire (0.125 in., 0.1% Na) was purchased from Alfa Inorganics and was washed with hexane prior to use. Mesitoic acid[27] and mesitoyl chloride[28] were synthesized from 2-bromomesitylene; the acid chloride was purified by careful vacuum distillation. Commercially available allylic alcohols were obtained from the following sources: allyl alcohol and *trans*-2-buten-1-ol (crotyl alcohol), Aldrich Chemical Co.; 3-buten-2-ol, 3-methyl-3-buten-2-ol, *cis*- (95%) and *trans*- (95%) 3,7-dimethyl-2,6-octadien-1-ol (nerol and geraniol, respectively), Chemical Samples Co.; 3-methyl-2-buten-1-ol[29] and 2-hydroxymethyl-1,3-butadiene[26] were prepared according to published methods. Two allylic bromides were commercially available: 1-bromo-3-methyl-2-butene, Chemical Samples Co.; allyl bromide, Matheson Coleman and Bell. Allylmagnesium bromide (2 M in THF) was purchased from Alfa Inorganics. All ketones and aldehydes used in the formation of carbinols were purchased and used without further purification. Both magnesium turnings and zinc dust used in carbinol synthesis were obtained from Mallinkrodt. Magnesium sulfate (MgSO₄) was employed as a drying agent in all cases. All boiling points are uncorrected. Nmr spectra were run on a Varian A-60 spectrometer, and all chemical shifts are given in parts per million downfield from internal TMS (δ scale). Infrared spectra were taken as neat films using a Perkin-Elmer Model 521 spectrophotometer. Elemental analyses were performed by the analytical service of the University of Illinois.

All glassware used for the *in situ* generation of allyllithiums was dried for at least 3 hr at 125°. Glass-coated stirring magnets were used in all cases, and a dry nitrogen atmosphere was maintained throughout the course of the reaction. Analytical glpc

(27) D. M. Bowen, "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 553.
(28) R. P. Barnes, ref 27, p 556.
(29) R. H. Hall and M. H. Fleysher in "Synthetic Procedures in Nucleic Acid Chemistry," W. W. Zorbach and R. S. Tipson, Ed., Wiley, New York. N. Y., 1968, p 517.

analyses were done on a Hewlett-Packard 5750 instrument fitted with flame ionization detectors using a carrier gas (N_2) flow of 30 ml/min. Product percentages were calculated from integrated peak area ratios, using *n*-alkanes with appropriate retention times as internal standards and correcting for differences in response factors. All analytical glpc columns have acid-washed, dimethyldichlorosilane-treated 80–100 mesh Chromosorb W as support and are referred to as follows: column A, 0.125 in. × 10 ft, 5% SE-30; column B, 0.125 in. × 6 ft, 10% UC-W98; column C, 0.125 in. × 3 ft, 5% SE-30; column D, 0.125 in. × 8 ft, 5% CW-4000; column E, 0.125 in. × 14 ft, 3% CW-4000; column F, 0.125 in. × 10 ft, 4.3% CW-4000.

All preparative glpc was done on a Varian Aerograph Model 90-P3 chromatograph with a thermal conductivity detector using a carrier gas (He) flow of 90 ml/min. The columns used are as follows: column G, 0.375 in. × 12 ft, 15% Carbowax 20M on 60–80 Chromosorb W; column H, 0.375 in. × 10 ft, 15% SE-30 on 60–80 Chromosorb W.

Synthesis of Mesitoates.—The mesitoates have been prepared by two general methods, denoted by A and B below, depending on the availability of the allylic alcohol. Specific cases are used to illustrate each method.

Method A. *trans*-3,7-Dimethyl-2,6-octadien-1-yl (Geranyl) Mesitoate.—Mesitoyl chloride (56.0 g, 0.307 mol) was dissolved in 80 ml of ethanol-free chloroform at 0°. Geraniol (55.6 g, 0.360 mol) and 43.6 g of dry pyridine were added over a 2-hr period. After stirring at room temperature for 72 hr, 300 ml of 10% hydrochloric acid was added, the organic layer was collected and washed with 10% NaOH and water, and solvent was removed under vacuum. Chromatography of the remaining oil on 400 g of neutral alumina using petroleum ether (bp 30–60°) gave 81.0 g (0.269 mol, 87.8% yield) of a clear oil: ir (neat) 1724 (s), 1078 cm^{-1} (s); nmr (CCl$_4$) δ 1.58–1.74 (m, 9 H), 2.08 (m, 4 H), 2.22 (s, 9 H), 4.69 (d, J = 8.0 Hz, 2 H), 5.01 (m, 1 H), 5.39 (t, J = 9.0 Hz, 1 H), 6.68 (s, 2 H).

Anal. Calcd for C$_{20}$H$_{28}$O$_2$: C, 79.96; H, 9.39. Found: C, 80.02; H, 9.39.

Method B. *trans*-2-Buten-1-yl (Crotyl) Mesitoate.—Mesitoyl chloride (56.0 g, 0.307 mol) was dissolved in 100 ml of ethanol-free chloroform. Crotyl alcohol (21.6 g, 0.300 mol) and 30.0 g of pyridine were dissolved in 50 ml of ethanol-free chloroform at 0° and added over a 1-hr period to the chloride. Stirring was continued at room temperature overnight, and 100 ml of water was added. The organic layer was washed twice with water, once with 10% HCl, and once with 5% NaHCO$_3$ (Caution: foaming) and dried. Solvent was removed under vacuum to leave a yellow oil which was vacuum distilled (103–104°, 0.2 Torr) to give 60.1 g (0.275 mol, 91.5% yield) of the desired ester: ir (neat) 1700 (s), 1242 (s), 1147 (s), 1055 cm^{-1} (s); nmr (CCl$_4$) δ 1.63 (m, 3 H), 2.19 (s, 9 H), 4.55 (m, 2 H), 5.69 (m, 2 H), 6.64 (s, 2 H).

Anal. Calcd for C$_{14}$H$_{18}$O$_2$: C, 77.03; H, 8.24. Found: C, 77.08; H, 8.24.

Allyl mesitoate (method A) (87.2% yield) had ir (neat) 1715 (s), 1257 (s), 1168 (s), 1078 cm^{-1} (s); nmr (CCl$_4$) δ 2.18–2.21 (m, 9 H), 4.67 (doublet of triplets, J_A = 5.5, J_B = 1.0 Hz, 2 H), 5.00–5.50 (m, 2 H), 5.90 (m, 1 H), 6.70 (s, 2 H).

Anal. Calcd for C$_{13}$H$_{16}$O$_2$: C, 76.43; H, 7.89. Found: C, 76.57; H, 7.79.

3-Methyl-2-buten-1-yl mesitoate (method A) (69.8% yield) had bp 138–139° (0.5 Torr); ir (neat) 1723 (s), 1265 (s), 1172 (s), 1083 cm^{-1} (s); nmr (CCl$_4$) δ 1.80 (m, 6 H), 2.22 (m, 9 H), 4.69 (d, J = 7.0 Hz, 2 H), 5.39 (t, J = 8.0 Hz, 1 H), 6.70 (s, 2 H).

Anal. Calcd for C$_{15}$H$_{20}$O$_2$: C, 77.55; H, 8.67. Found: C, 77.60; H, 8.66.

cis-3,7-Dimethyl-2,6-octadien-1-yl (neryl) mesitoate (method A) (79.2% yield) had ir (neat) 1720 (s), 1611 (s), 1444 (s), 1379 (m), 1261 (s), 1169 (s), 1078 cm^{-1} (s); nmr (CCl$_4$) δ 1.60–1.76 (m, 9 H), 2.16 (m, 4 H), 2.28 (s, 9 H), 4.76 (d, J = 8.0 Hz, 2 H), 5.12 (m, 1 H), 5.48 (t, J = 7.0 Hz, 1 H), 6.68 (s, 2 H).

Anal. Calcd for C$_{20}$H$_{28}$O$_2$: C, 79.96; H, 9.39. Found: C, 80.20; H, 9.44.

3-Methyl-1-buten-3-yl mesitoate (method B) (69.2% yield) had bp 108–110° (0.8 Torr); ir (neat) 1736 (s), 1276 (s), 1086 cm^{-1} (s); nmr (CCl$_4$) δ 1.60 (s, 6 H), 2.17–2.30 (m, 9 H), 4.87–5.38 (m, 2 H), 6.24 (doublet of doublets, J_A = 18.0, J_B = 10.4 Hz, 1 H), 6.72 (s, 2 H).

Anal. Calcd for C$_{15}$H$_{20}$O$_2$: C, 77.55; H, 8.68. Found: C, 77.50; H, 8.70.

1-Buten-3-yl mesitoate (method B) (73.4% yield) had bp 94.5–95.0 (0.7 Torr); ir (neat) 1726 (s), 1265 (s), 1082 cm^{-1} (s); nmr (CCl$_4$) δ 1.40 (d, J = 6.6 Hz, 3 H), 2.28 (m, 9 H), 5.00–6.25 (m, 4 H), 6.74 (s, 2 H).

Anal. Calcd for C$_{14}$H$_{18}$O$_2$: C, 77.03; H, 8.31. Found: C, 76.80; H, 8.41.

Allylic Bromides.—Geranyl, neryl, farnesyl, and *trans*-2-butenyl bromides were prepared by the action of phosphorus tribromide (PBr$_3$) on the corresponding carbinols and gave a positive test with alcoholic silver nitrate. All bromides were stored at −20°, as decomposition was quite rapid at room temperature. The synthesis of geranyl bromide is typical of the method used.

trans-3,7-Dimethyl-2,6-octadienyl (Geranyl) Bromide.—Geraniol (44.5 g, 0.288 mol) was dissolved in 250 ml of dry ether at 0°, and PBr$_3$ (32.4 g, 0.12 mol) was added dropwise. After 3 hr, ice water was added, the organic layer was collected and dried, and solvent was removed under vacuum to give 56.8 g (0.262 mol, 91% yield) of a pale yellow oil: nmr (CCl$_4$) δ 1.70 (m, 9 H), 2.08 (m, 4 H), 3.94 (d, J = 11.0 Hz, 2 H), 5.08 (m, 1 H), 5.5 (t, J = 9.0 Hz, 1 H).

Coupling Reactions (General Procedure).—The allylic bromide (0.01 mol) was added to the allylic mesitoate (0.01 mol) in 50 ml of dry THF. An excess of freshly cut lithium (*ca.* 0.1 g-atom, 0.1% Na) was added, and the reaction flask was evacuated and flushed several times with dry nitrogen. Stirring was done using a glass-coated stirring bar, and the reaction was kept at 0° until a deep red-brown color formed. The reaction was quenched by addition of 1 ml of water, and the mixture was immediately filtered through glass wool into 50 ml of 5% NaOH and 50 ml of ether. The aqueous layer was isolated and acidified (concentrated HCl) to give mesitoic acid, while the organic layer was collected and dried. Products were identified either by isolation or by comparison with a known sample.

trans-2,6-Dimethyl-2,6,10-undecatriene (1a, 1g) was obtained from allyl mesitoate and geranyl bromide; yield 22% as determined by glpc using internal standard. Retention times (glpc) were identical with those of an authentic sample prepared from allylmagnesium bromide and geranyl bromide: column C (130°), 1.6 min; column B (105°), 4.9 min. From geranyl mesitoate and allyl bromide, the yield of coupled products was 60% from glpc. From a preparative scale reaction using the same components, the olefin fraction was isolated by chromatography over alumina using hexane. Glpc showed a 35% yield of cross-coupled products. An analytical sample was isolated by preparative glpc (column H) and gave glpc retention times and nmr spectra identical with those of the authentic sample: nmr (CCl$_4$) δ 1.52–1.78 (m, 9 H, –CH$_3$), 1.95–2.17 (m, 8 H, –CH$_2$–), 4.69–5.21 (m, 4 H), 5.30–6.10 (m, 1 H).

Anal. Calcd for C$_{11}$H$_{22}$: C, 87.56; H, 12.44. Found: C, 87.62; H, 12.18.

trans,trans-2,6-Dimethyl-2,6,10-dodecatriene (1f) was obtained from crotyl mesitoate and geranyl bromide; the yield of cross-coupled products was 19% as determined by glpc using internal standards. Retention times were found to be identical with those of an authentic sample prepared by coupling crotyl and geranyl bromides over magnesium: column C (130°), 2.8 min; column G (195°), 4.0 min. A sample isolated from mesitoate reaction by preparative glpc (column G) gave the following spectral data: nmr (CCl$_4$) δ 1.50–1.70 (m, 12 H, –CH$_3$), 1.85–2.14 (m, 8 H, –CH$_2$–), 4.85–5.50 (m, 4 H, olefinic H).

trans-2,6,11-Trimethyl-2,6,10-dodecatriene (1b, 1e) was obtained from 3-methyl-2-butenyl bromide and geranyl mesitoate; preparative-scale reaction using 0.08 mol of each reactant gave a 49% yield of cross-coupled dienes. Preparative glpc (column H) was used to isolate the triene, which gave the following spectral and analytical data: nmr (CCl$_4$) δ 1.50–1.72 (m, 15 H, –CH$_3$), 1.95 (m, 8 H, –CH$_2$–), 5.03 (m, 3 H, olefinic H).

Anal. Calcd for C$_{15}$H$_{26}$: C, 87.30; H, 12.70. Found: C, 87.15; H, 12.60.

From 3-methyl-2-butenyl mesitoate and geranyl bromide, the yield of cross-coupled products was 32%. The product was identified by comparison with a known sample on glpc: column B (170°), 3.5 min; column C (160°), 4.6 min.

trans,trans,trans-2,6,10,15,19-Pentamethyl-2,6,10,14,18-eicosapentaene (1d) was obtained from geranyl mesitoate and farnesyl bromide; the yield of cross-coupled products was 43% as shown by glpc using an internal standard. Retention times were found to be identical with those of an authentic sample prepared by coupling geranyl and farnesyl bromides over magnesium: column C (220°), 4.0 min.

Both C_{20} (Ger–Ger) and C_{30} (Far–Far) products formed in the mesitoate and magnesium (Wurtz) couplings of geranyl and farnesyl units were identified by glpc comparison to geranyl dimers[12] and a known sample of farnesyl dimer (squalene), respectively.

Coupling of Neryl–Geranyl, Neryl–Neryl, and Geranyl–Geranyl Units.—Digeranyl (1c) and isodigeranyl (2c) were prepared by the method of Barnard and Batemann[12] and were used as knowns for glpc identification. These compounds were obtained in 95% yield from reaction of 0.01 mol of geranyl mesitoate and 0.01 mol of geranyl bromide using glpc internal standards to determine the yield. A preparative-scale reaction using 0.10 mol of each component gave an isolated yield of 93% of the coupled products. These were identified by comparison to the known samples on glpc (Column A, 260°): digeranyl (1c), 4.8 min; isodigeranyl (2c), 2.1 min.

The dienes 3 and 5 were assigned the structures given, as they are the expected coupling products of two neryl units (based on analogy to what is known for the coupling of two geranyl units). Glpc retention times of these 1,5-dienes (column A, 260°) are as follows: dineryl (3), 4.2 min; isodineryl (5), 3.8 min.

The 1,5-diene 5 was assigned its structure, as it is the expected main coupling product to be formed in a coupling reaction between a neryl and a geranyl unit. Glpc retention time of this compound (column A, 260°) was 4.5 min. Yields of these compounds from the mesitoate coupling reactions were determined using internal standards.

Reaction of Mesitoic Acid with Lithium.—Mesitoic acid (3.4 g, 0.021 mol) was dissolved in 70 ml of dry THF. A large excess of freshly cut lithium chips (*ca.* 0.2 mol) was added, and the mixture was allowed to stir at 25° for 17 hr. The resulting deep red solution was transferred by means of a polyethylene tube to a flask containing 6.0 ml of methyl iodide, and after 10 min, the organic layer was diluted with 50 ml of ether and extracted twice with base (5 *M* NaOH) to remove any acidic material. The organic layer was dried and solvent was removed to give 1.7 g of a yellow oil shown by glpc to contain at least six components, three of which constituted about 85% of the total. Methyl (2,4,6-trimethylphenyl)methyl ether (6) and methyl (4-ethyl-2,6-dimethylphenyl) methyl ether (7), two of the three major products, were isolated together by column chromatography (alumina) using ligroin followed by ethyl ether. By glpc–mass spectral analysis (column A, 145°), compound 6 was shown to have a molecular weight of 164 and 7 a molecular weight of 178. Both compounds showed a large P − 32 peak. The structure of 6 was confirmed by an independent synthesis from 2,4,6-trimethylbenzyl alcohol and methyl iodide. The structure of 7 was inferred from the mass spectrum and the nmr spectrum.

Compound 6 had nmr (CCl₄) δ 2.11 (s, 3 H), 2.17 (s, 6 H), 3.12 (s, 3 H), 4.18 (s, 2 H), 6.71 (s, 2 H); mass spectrum (70 eV) *m/e* (rel intensity) 164 (7), 149 (16), 133 (50), 132 (100), 117 (30), 105 (15), 91 (18).

Compound 7 had nmr (CCl₄) δ 1.08 (t, *J* = 4.0 Hz, 3 H), 2.11–2.17 (m, 6 H), 2.61 (q, *J* = 4.0 Hz, 2 H), 3.14 (s, 3 H), 4.18 (s, 2 H), 6.72 (s, 2 H); mass spectrum *m/e* (rel intensity) 178 (2), 163 (8), 157 (32), 146 (100), 132 (22), 131 (70), 105 (15), 91 (25).

Reduction of Allyl Mesitoate with Lithium.—Allyl mesitoate (2.94 g, 0.014 mol) was dissolved in 50 ml of THF, and an excess of lithium (*ca.* 0.15 g-atom) was added. After stirring for 24 hr at room temperature, the resulting dark red solution was transferred to a flask containing 15 ml of THF and 5 ml of methyl iodide. After reaction was complete, 50 ml of ether was added, and the mixture was extracted with 25 ml of 5 *M* NaOH solution. Acidification of the aqueous layer gave only a trace of mesitoic acid. Glpc–mass spectral analysis of the organic layer (column C) showed at least 13 compounds with a molecular weight range of 134–246. Only one of these, 8, was identified by comparison to published mass spectral data.[30] No structures have been assigned to the remaining compounds.

In a separate experiment, 0.02 mol (2.08 g) of allyl mesitoate was mixed with 50 ml of dry THF, and an excess of lithium was added. Stirring was done under a dry nitrogen atmosphere at 0° with a glass-coated stirring bar. At the time intervals shown in Figure 1, 2.0-ml aliquots were withdrawn and injected into an inverted buret to measure the evolution of propene (and thus allyllithium). At no point did the volume of propene exceed

(30) "Eight Peak Index of Mass Spectra," 1st ed, Vol. I, Mass Spectrometry Data Centre, Aldermaston, Reading, U. K., 1970, p 102.

2.05 ml at STP (theoretical amount of gas formed if allyllithium was formed quantitatively was 17.9 ml). The reaction was monitored in such a fashion for 18 hr; glpc analysis indicated complete consumption of allyl mesitoate within 1.5 hr.

1-(2,4,6-Trimethylphenyl)-*trans*-2-buten-1-one (9).—Allyllithium, prepared from 10.0 g of allyl phenyl ether,[8] was added to allyl mesitoate (1.5 g, 0.0074 mol) in 5 ml of THF at room temperature. After stirring for 15 min, water was added; the organic layer was dried, and solvent was removed under vacuum. The ketone 9 was isolated by preparative tlc on silica gel using ether–hexane (1:9) to give 0.9 g (65% yield) of a clear oil: ir (neat) 2921 (w), 1659 (s), 1437 (w), 1282 cm⁻¹ (m); nmr (CCl₄) δ 1.86 (d, *J* = 5.2 Hz, 3 H), 2.11 (s, 6 H), 2.26 (s, 3 H), 6.01–6.57 (m, 2 H), 6.75 (s, 2 H).

Anal. Calcd for C₁₃H₁₆O: C, 82.94; H, 8.57. Found: C, 82.68; H, 8.44.

Synthesis of Allylic Carbinols.—Each of the allylic carbinols was synthesized both by one of two Reformatsky-type procedures (method A, magnesium; method B, zinc) and by the mesitoate-lithium procedure (method C). The three methods are illustrated by the first three procedures given below.

In several cases with the Reformatsky method, no boiling points are reported for the distillation, as severe foaming occurred. In such cases, after crude distillation to give a fraction of about 95% purity, preparative glpc followed by molecular distillation was used to prepare a sample for spectroscopic analysis and microanalysis.

Method A (Magnesium). 1-Allylcyclohexanol (13).—Magnesium (14.4 g, 0.59 g-atom) was added to 500 ml of dry ether along with a few crystals of iodine. A small amount (<1 ml) of allyl bromide was added, and after Grignard formation had begun, the solution was cooled to 0°. A mixture of cyclohexanone (28.0 g, 0.255 mol) and allyl bromide (35.3 g, 0.28 mol) was then added dropwise over a 2-hr period. The reaction was allowed to stir overnight at 25°, and water was then added to quench the reaction. The aqueous layer was washed twice with ether and the combined organic layers were dried and placed under vacuum for solvent removal to give a clear liquid product. Distillation gave 33.8 g (0.242 mol, 95% yield) of the desired carbinol: bp 81–82° (9.0 mm) [lit.[22] bp 70–72° (8.0 mm)]; ir (neat) 3495 (m), 3080 (w), 2937 (s), 1638 (m), 1448 (m), 971 (m), 909 cm⁻¹ (m); nmr (CCl₄) δ 1.47 (s, 10 H), 2.16 (doublet of triplets, J_A = 7.0, J_B = 1.0 Hz, 2 H), 2.25 (s, 1 H), 5.00 (m, 2 H), 5.83 (m, 1 H).

Anal. Calcd for C₉H₁₆O: C, 77.09; H, 11.50. Found: C, 77.10; H, 11.47.

Compound 13 was also prepared by method C from allyl mesitoate and cyclohexanone, 42% yield. A 56% yield was obtained by using 0.02 mol (2 equiv) of the mesitoate with 0.01 of the ketone. 13 was identified by comparison to a known sample on glpc: column A (145°), 2.3 min; column B (122°), 3.2 min.

Method B (Zinc). 1-Decen-4-ol (17).—To 200 ml of dry ether was added heptanal (51.5 g, 0.451 mol) and dry zinc dust (39.2 g, 0.60 g-atom). A small amount (5.0 g) of the total amount of allyl bromide (54.5 g, 0.451 mol) was added, and stirring was continued until vigorous reflux indicated the start of the reaction. The remaining bromide was added at such a rate so as to maintain vigorous reflux, and after the addition was complete, the reaction was allowed to stir for an additional 2 hr. The reaction mixture was quenched by slow addition to 500 ml of dilute hydrochloric acid, and the hydrolysate was stirred until most of the inorganic material had dissolved. The mixture was filtered, and the organic layer was collected, dried, concentrated, and vacuum distilled to give 48.6 g (0.312 mol, 69% yield) of the desired carbinol: bp 65.4–66.0° (0.16 mm); ir (neat) 3350 (m), 3080 (w), 2960 (m), 2930 (s), 2861 (s), 1639 (s), 1461 (m), 992 (w), 991 cm⁻¹ (m); nmr (CCl₄) δ 0.90 (m, 3 H, –CH₃), 1.33 (s, 10 H), 2.18 (m, 2 H), 2.65 (s, 1 H, –OH), 3.57 (m, 1 H, –CHOH), 4.82–5.20 (m, 2 H), 5.50–6.20 (m, 1 H).

Anal. Calcd for C₁₀H₂₀O: C, 76.86; H, 12.90. Found: C, 76.92; H, 12.93.

Compound 17 was also prepared by method C from allyl mesitoate and heptanal, 14% yield. It was compared to a known sample on glpc: column C (110°), 2.6 min.

Method C (Lithium–Mesitoate). 1-[3-(1-Butenyl)]-cyclohexanol (14).—To a mixture of 2.18 g (0.01 mol) of 2-buten-1-yl mesitoate and 0.98 g (0.01 mol) of cyclohexanone in 25 ml of THF was added an excess of freshly cut lithium (*ca.* 0.1 mol). The reaction mixture was stirred under a dry nitrogen atmosphere at 0° for about 1 hr. The reaction mixture (dark green) was

filtered through glass wool into a mixture of 50 ml of dilute sodium hydroxide solution and 50 ml of ether. The organic layer was collected and dried, internal standard was added for glpc yields, and solvent was removed by vacuum to give a 39% yield of **14** by glpc analysis.

14 was also prepared from 3-(1-butenyl) mesitoate and cyclohexanone, 35% yield, and compared to a known sample (prepared by method B, below) on glpc: column E (170°), 5.2 min; column B (139°), 4.1 min. A sample was isolated by preparative glpc (column H) from the 2-buten-1-yl mesitoate reaction and gave an nmr identical with that of the known sample.

Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.87; H, 11.56.

Compound **14** was also prepared by method B from cyclohexanone and 1-bromo-2-butene in 72% yield: purified after distillation by preparative glpc, column H; ir (neat) 3450 (m), 3078 (w), 2939 (s), 2860 (m), 1449 (w), 949 (w), 908 cm⁻¹ (w); nmr (CCl₄) δ 1.00 (d, J = 6.4 Hz, 3 H), 1.18–1.80 (m, 11 H, –CH₂–, –OH), 2.13 (m, 1 H), 4.80–5.17 (m, 2 H), 5.53–6.15 (m, 1 H).

Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; 11.76. Found: C, 77.98; H, 11.59.

1-[3-(3-Methyl-1-butenyl)]cyclohexanol (15) (method A) was obtained from cyclohexanone and 3-methyl-2-butenyl bromide: 73% yield; bp 66.5–67.5° (1.5 mm); ir (neat) 3497 (m), 2941 (s), 2861 (m), 1632 (w), 1449 (w), 1130 (w), 961 (m), 911 cm⁻¹ (m); nmr (CCl₄) δ 1.00 (s, 6 H), 1.27 (s, 1 H, –OH), 1.32–1.85 (m, 10 H), 4.71–5.13 (m, 2 H), 5.68–6.22 (doublet of doublets, 1 H).

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.41; H, 11.80.

Compound **15** was also prepared by method C from 3-methyl-2-butenyl mesitoate and cyclohexanone, 22% yield, and from 3-(3-methyl-1-butenyl) mesitoate and cyclohexanone, 25% yield. It was compared to a known sample (prepared above by method A) on glpc: column A (145°), 4.6 min; column B (162°), 3.1 min.

1-Allylcyclopentanol (16) (method A) was obtained from cyclopentanone and allyl bromide: 80% yield; bp 66–67.5° (14 mm); ir (neat) 3389 (s), 3078 (m), 2950 (s); 2876 (s), 1638 (s), 1432 (m), 1182 (m), 989 (s), 909 cm⁻¹ (s); nmr (CCl₄) δ 1.58 (s, 8 H), 2.25 (doublet of triplets, J_A = 7.0 Hz, J_B = 1.0 Hz, 2 H), 2.60 (s, 1 H, –OH), 4.75–5.20 (m, 2 H), 5.49–6.20 (m, 1 H).

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.19; H, 11.12.

Compound **16** was also prepared by method C from allyl mesitoate and cyclopentanone, 27% yield. It was compared to a known sample (prepared above) on glpc: column F (95°), 3.1 min; column A (125°), 2.2 min.

2-Methyl-3-isopropyl-5-hexen-3-ol (18) was prepared by direct addition of 70 ml of 2 M allylmagnesium chloride (0.14 mol) in THF to 11.5 g (0.10 mol) of diisopropyl ketone in 150 ml of dry THF at 0°. After stirring for 12 hr at 25°, the reaction mixture was quenched by slowly adding to 100 ml of dilute hydrochloric acid. The organic layer was isolated and dried, and solvent was removed by vacuum. The remaining liquid was distilled under reduced pressure (91–95°, 30 mm) to give 11.8 g (0.0754 mol, 75.4% yield) of the desired carbinol. An analytical sample was prepared by preparative glpc (column H) followed by bulb-to-bulb distillation: ir (neat) 3500 (m), 3080 (w), 2968 (s), 1637 (w), 1468 (m), 1376 (m), 1096 (w), 991 (m), 977 (m), 910 cm⁻¹ (m); nmr (CCl₄) 0.91 (doublet of doublets, J_A = 7.8, J_B = 1.7 Hz, 12 H), 1.25 (s, 1 H), 1.50–2.08 (m, 2 H), 2.12–2.31 (m, 2 H), 4.73–5.17 (m, 2 H), 5.46–6.14 (m, 1 H).

Anal. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.88; H, 12.75.

18 was also prepared by method C using allyl mesitoate and diisopropyl ketone, 60% yield. It was compared to a known sample on glpc: column A (145°), 2.7 min; column B (170°), 1.5 min.

2,2-Dimethyl-3-hydroxy-5-hexene (19) (method B) was obtained from pivaldehyde and allyl bromide, 84% yield. A sample was prepared by preparative glpc, column G: ir (neat) 3439 (s), 3079 (m), 2951 (s), 2872 (s), 1638 (s), 1479 (s), 1363 (s), 1291 (m), 1071 (s), 1000 (s), 910 (s), 861 cm⁻¹ (m); nmr (CCl₄) δ 0.88 (s, 9 H), 1.58–2.53 (m, 3 H, –CH₂–, –OH), 3.18 (doublet of doublets, J_A = 10.0, J_B = 2.8 Hz, 1 H), 4.77–5.20 (m, 2 H), 5.46–6.18 (m, 1 H).

Anal. Calcd for $C_8H_{16}O$: C, 74.94; H, 12.58. Found: C, 74.99; H, 12.34.

Compound **19** was also prepared by method C from pivaldehyde and allyl mesitoate, 64% yield. It was compared to an authentic sample (prepared above) on glpc: column A (120°), 2.0 min; column B (128°), 1.5 min. A preparative-scale reaction using 0.03 mol of each reagent gave an isolated yield of **19** of 49%. An nmr identical with that of the authentic alcohol was obtained from this sample.

endo-**1,3,3-Trimethyl-2-allylbicyclo[2.2.1]heptan-2-ol (20) (method A)** was obtained from fenchone and allyl bromide, 50% yield. An analytical sample was prepared by preparative glpc (column H) as the reaction mixture could not be successfully fractionated: ir (neat) 3575 (m), 3080 (w), 2959 (s), 2881 (s), 1632 (m), 1467 (m), 1369 (m), 1063 (m), 994 (m), 923 cm⁻¹ (m); nmr (CCl₄) δ 0.85 (s, 3 H), 0.97 (s, 3 H), 1.03 (s, 3 H), 1.12–2.60 (m, 10 H), 4.85–5.21 (m, 2 H), 5.60–6.29 (m, 1 H).

Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.35; H, 11.29.

Compound **20** was also prepared by method C from fenchone and allyl mesitoate, 67% yield, and compared to a known sample (prepared above) on glpc: column A (152°), 5.8 min; column B (163°), 4.7 min.

2,2-Dimethyl-3-hydroxy-3-*tert*-butyl-5-hexene (21) (method A) was obtained from di-*tert*-butyl ketone and allyl bromide: 75% yield; bp 130–135° (21 mm); ir (neat) 3585 (m), 3081 (m), 2962 (s), 1485 (s), 1396 (s), 1374 (s), 1210 (m), 1076 (m), 1004 (m), 922 cm⁻¹ (m); nmr (CCl₄) δ 1.02 (s, 18 H), 1.36 (s, 1 H, –OH), 2.41 (m, 2 H), 4.73–5.14 (m, 2 H, –C=CH₂), 5.51–6.10 (m, 1 H).

Anal. Calcd for $C_{12}H_{24}O$: C, 78.20; H, 13.12. Found: C, 78.29; H, 13.03.

Compound **21** was also prepared by method C from allyl mesitoate and di-*tert*-butyl ketone, 54 and 52% yields in consecutive experiments. **21** was compared to a known sample (prepared above) on glpc: column F (136°), 2.0 min; column A (155°), 3.8 min.

2-Methyl-6-methylene-7-octen-4-ol (24) (method B).—To a mixture of 2-bromomethyl-1,3-butadiene[26] (5.0 g, 0.034 mol) and isovaleraldehyde (2.94 g, 0.034 mol) in 40 ml of dry THF was added 3.0 g (0.046 g-atom) of zinc. After refluxing for 4 hr, the entire reaction mixture was poured into a mixture of water and ether and filtered to remove inorganic salts, and the organic layer was dried and concentrated. The remaining oil was distilled (bulb to bulb, 1.5 mm, 150°) to give 2.7 g (0.0175 mol, 52% yield) of the alcohol **24**: ir (neat) 3480 (m), 3089 (w), 2960 (s), 1596 (m), 1468 (m), 1388 (w), 1368 (w), 1071 (w), 1023 (w), 993 (m), 898 cm⁻¹ (s); nmr (CCl₄) δ 0.92 (doublet of doublets, J_A = 7.0, J_B = 2.1 Hz, 6 H), 1.28 (m, 2 H), 1.72 (m, 1 H), 2.12–2.38 (m, 3 H, –CH₂–, –OH), 3.74 (m, 1 H, –CHOH), 5.01–5.38 (m, 4 H), 6.31 (doublet of doublets, J_A = 17.0, J_B = 10.0 Hz, 1 H).

Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 78.07; H, 11.67.

Compound **24** was also prepared by method C from 2-(mesityloxymethyl)-1,3-butadiene (**23b**) and isovaleraldehyde (**22**); the attractant **24** was isolated by preparative tlc on silica gel using ether–hexane (1:10) to give a 10.0% yield. The material was identified by comparison to a known sample (prepared by method B) on glpc: column A (138°), 2.9 min; column B (150°), 2.1 min.

The Nickel(0)-Catalyzed Addition of Phenol to Butadiene

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The (organophosphorus)nickel(0)-catalyzed reaction of phenol and butadiene gives mixtures of 3-phenoxy-1-butene, 1-phenoxy-2-butene, 3-phenoxy-1,7-octadiene, and 1-phenoxy-2,7-octadiene. The formation of phenoxy-butenes is favored by electron-donor ligands, excess ligand, high phenol concentration, and low conversions. A mechanism based on dual reaction pathways for an (organophosphorus)nickel intermediate is presented to explain these results.

Mechanistic understanding of transition metal catalyzed reactions is far behind other fields of chemistry. Recently elegant studies have elucidated some details by isolation and identification of intermediates in catalytic cycles.[1-3] Hopefully the concepts developed in such pioneering work can be broadly applied to related reactions.

Phenol reacts with butadiene in the presence of tetrakis(organophosphorus)nickel(0) to give 3-phenoxy-1-butene, *trans*-1-phenoxy-2-butene, 3-phenoxy-1,7-octadiene, and *cis*- and *trans*-1-phenoxy-2,7-octadiene.[4]
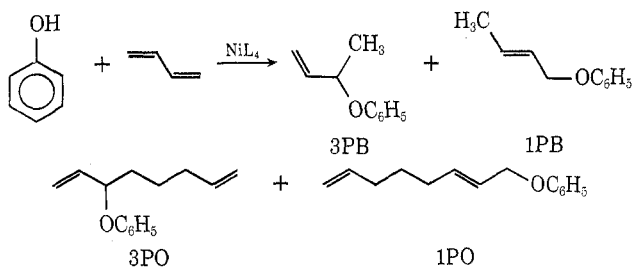
The goal of this work was to optimize the formation of the phenoxybutenes, as palladium seems to be a superior catalyst for the synthesis of phenoxyoctadienes.[4,5]

Experimental Section

Analytical Runs.—A Pyrex tube was sealed with a serum stopper and evacuated. Butadiene was distilled into the tube at $-78°$ from a calibrated reservoir. Solutions of phenol in ether, nickelocene in benzene, and ligand were injected *via* syringe and the tube was sealed. The order of addition was immaterial. After warming to room temperature the tubes were heated and agitated in a thermostatted oven. After the desired reaction time the tubes were cooled to $-78°$ and opened, and the contents were examined by gas chromatography on a 6 ft × 0.25 in. column of 20% silicone 200 supported on Gas-Chrom RA (60–80) at 180° and 75 ml/min. The retention times (minutes) follow: phenol, 1.0; 3PB, 1.7; 1PB, 2.7; 3PO, 7.2; and 1PO, 11.7. Areas were calculated using triangular approximation of peak height times line width. Standards prepared using materials purified by preparative gas chromatography showed that area per cent calculated in this way corresponded closely to mole per cent. Precision is estimated at ±3% for duplicate runs; accuracy is undoubtedly lower.

Catalyst cycles are defined as moles of products per mole of nickel charged. The yield of the phenoxybutenes and phenoxyoctadienes is essentially quantitative based on phenol consumed.

Preparative Runs.—A Hastelloy C bomb was charged under nitrogen with solutions of ligand, nickelocene, and phenol in ether. The bomb was sealed, evacuated, and charged with butadiene. After the reaction was complete excess butadiene was vented and the remaining contents were discharged. The ether solution was extracted with sodium hydroxide until gc showed the absence of phenol. After removal of most of the solvent, the residue was distilled through a Nestor-Faust spinning-band column at reduced pressure. Four fractions were obtained: fraction 1, 3-phenoxy-1-butene, bp 37–40° (1 mm), n^{25}D 1.5072 [lit.[6] bp 43° (0.8 mm)]; fraction 2, 1-phenoxy-3-butene, bp 58–59° (1 mm), n^{25}D 1.5173 [lit.[6] bp 87° (8 mm)]; fraction 3, 3-phenoxy-1,7-octadiene, bp 87° (1 mm), n^{25}D 1.5077; fraction 4, 1-phenoxy-2,7-octadiene, bp 104° (1 mm), n^{25}D 1.5153. The proton nmr spectrum of fraction 4 suggested the presence of 15% cis and 85% trans isomers.[4] No attempt was made to separate these two compounds.

Phosphorus ligands and nickel(0) complexes were obtained from the same sources cited by Tolman.[7]

The results of the studies of several reaction variables are presented individually followed by discussion in terms of a single mechanistic proposal.

Temperature-Time.—Time studies at 100° with tetrakis(triphenylphosphite)nickel catalyst showed that the reaction was essentially complete after 2 hr, and the product composition was unchanged on extended heating. Higher temperatures gave lower conversions to the four addition products and new peaks began to appear in the gas chromatograms. Although these products have not been isolated and identified, they may result from phenol alkylation rather than addition.[4] Heating for 15 hr at 90° gave essentially identical yields and conversions as runs at 100°, but lower temperatures showed a sharp discontinuity. The product distribution at various temperatures for 15 hr is summarized in Table I while the product distribution as a function of time at 70° is given in Table II.

There is an induction period before the rapid formation of phenoxyoctadienes begins. The absolute amount of phenoxybutenes does not decline during this rapid formation of phenoxyoctadienes, but steadily increases. At low conversion the yield of 3PB is greater than that of 1PB, but later the relative amount of 1PB increases.

(1) (a) Hydroformylation: R. F. Heck, *Advan. Organometal. Chem.*, **4**, 243 (1966). (b) Palladium-catalyzed oxidations: A. Aguiló, *ibid.*, **5**, 321 (1967).

(2) (a) Rhodium-catalyzed ethylene dimerization: R. Cramer, *J. Amer. Chem. Soc.*, **87**, 4717 (1965). (b) Nickel-catalyzed addition of ethylene to butadiene: C. A. Tolman, *ibid.*, **92**, 6777 (1970).

(3) For a review of the chemistry of butadiene with nickel(0) see P. Heimbach, P. W. Jolly, and G. Wilke, "Advances in Organometallic Chemistry," Vol. 8, Academic Press, New York, N. Y., 1970, pp 29–86.

(4) E. J. Smutny, H. Chung, K. C. Dewhirst, W. Keim, T. M. Shryne, and H. E. Thyret, *Amer. Chem. Soc., Div. Petrol. Chem., Prepr.*, 14 (2), B100–B111 (1969); H. Chung and W. Keim, U. S. Patent 3,636,162 (1969).

(5) Since the completion of this work, T. C. Shields and W. E. Walker, *Chem. Commun.*, 193 (1971), have described experiments in this area.

(6) H. L. Goering and R. R. Jacobson, *J. Amer. Chem. Soc.*, **80**, 3277 (1958).

(7) C. A. Tolman, *ibid.*, **92**, 2956 (1970).