Palladium-Catalyzed Vinyl Substitution Reactions. I. A New Synthesis of 2- and 3-Phenyl Substituted Allylic Alcohols, Aldehydes, and Ketones from Allylic Alcohols

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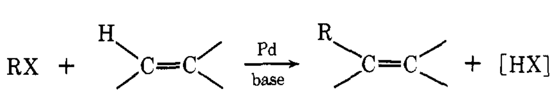
The palladium-catalyzed arylation of olefins has been extended to allylic alcohols. Aldehydes are formed from primary, ketones from secondary, and aryl-substituted allylic alcohols from tertiary allylic alcohols. With iodobenzene, a variety of organic and inorganic bases may be employed, but with bromobenzene, sodium bicarbonate is preferred.

The palladium-catalyzed substitution of vinylic hydrogen by aryl and vinyl halides was discovered by Mizoroki and co-workers[1] and Heck et al.[2,3] (reaction 1).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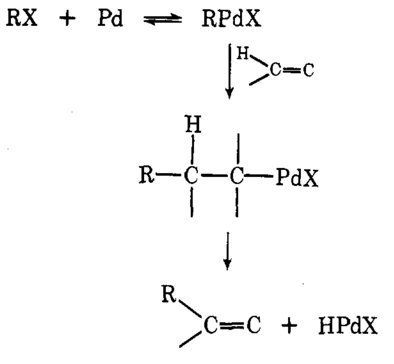
The reaction was reported to tolerate a variety of functional groups and examples were given of aryl halides with the substituents OMe, COOMe, NO_2, Cl, and C_6H_5. The olefins employed were limited to styrene, 4-nitrostyrene, 1-phenyl-1-propene, ethylene, propylene, 1-hexene, and methyl acrylate. Yields were reported to be low for olefins having methylene groups adjacent to the double bond.[2]

The mechanism of the reaction involves the formation of an organopalladium halide by an oxidative addition followed by addition to the olefin and elimination of HPdX.


(2a)

(2b)

(2c)

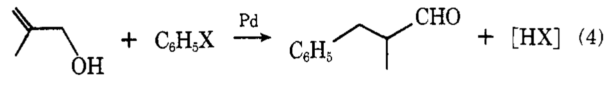
$$\text{HPdX} + \text{base} \longrightarrow \text{base HX} + \text{Pd} \quad (2d)$$

The organopalladium species may be generated by other means, such as reaction 3, which was used earlier by Heck.[4]

$$C_6H_5HgCl + PdCl_2 \rightleftharpoons C_6H_5PdCl + HgCl_2 \quad (3)$$

Under the mild conditions possible with 3, the phenylpalladium species was capable of reacting with a wide variety of olefins and in particular gave aldehydes and ketones with allylic alcohols.[5] We therefore were intrigued with the possibility of achieving a similar successful synthesis of aldehydes and ketones by the use of allylic alcohols in reaction 1.

Since reaction 2a requires considerably higher temperatures than reaction 3, we expected problems with side reactions, particularly those induced by base. Tertiary amines could deactivate the catalyst either by competing with the olefin for coordination sites, promoting the formation of inactive π-allyl complexes, or by catalyzing aldol condensations in the product aldehydes. We therefore first examined the effect of a variety of bases on the reaction of methallyl alcohol with bromo- and iodobenzene with the hope of achieving the following reaction.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Upon finding satisfactory conditions for reaction 4 a variety of allylic alcohols were then treated with iodobenzene and bromobenzene. A subsequent paper will discuss the effect of substituents on the aryl halide and the reaction of halobenzenes with nonallylic unsaturated alcohols.

Results

1. Reaction of Halobenzenes with Methallyl Alcohol. Table I gives results for reaction 4 where X = I and X = Br, respectively. Reasonable yields were obtained under a variety of conditions and this flexibility was later of value when the reaction was extended to other unsaturated alcohols and substituted aryl halides which imposed greater restraints on the synthesis.

The greatest reactivity was found for X = I, and when a hindered tertiary amine was used there was a spontaneous exotherm when the reaction was raised to 100°. Biphenyl was a side product whose yield was promoted by the presence of the polar aprotic solvent hexamethylphosphoramide (HMP) when diisopropylethylamine was used as base. In the absence of solvent, a good yield of 1 was obtained using diisopropylethylamine (85%). Lower yields were obtained with less hindered tertiary amines (e.g., morpholine, 60%). For the weaker bases the reaction was much slower. Diethylaniline gave rise to a weak exotherm and gave 40% conversion in 30 min at 130° but thereafter both 1 and the amine decreased in concentration, presumably owing to a condensation between the two. Para-substituted diethylanilines (-CN, -COPh) gave no reaction. Pyridine and 2,6-lutidine also gave no significant reaction, probably owing to the formation of complexes which were too stable to be catalytically active. Some sodium salts of weak acids were also successfully used as bases, providing that polar aprotic solvents were used (e.g., HMP or *N*-methylpyrrolidinone, NMP). Sodium bicarbonate gave significantly faster rates and yields than sodium acetate. The addition of triphenylphosphine made little difference to these reactions.

By contrast, only traces of 1 were formed from bromobenzene when triethylamine was used as base. Slightly better results were obtained with the more hindered base, diisopropylethylamine, but in both cases the principal product was an unidentified mixture of high-boiling materials. These were not, however, formed by a simple base-catalyzed condensation of the aldehyde which was found to be stable to tertiary amines at the temperatures used. A vari-

Table I
Reaction of Iodobenzene and Bromobenzene with Methallyl Alcohol[a]

Base	Halogen	Temp, °C	Time, hr	Solvent	Conversion,[b] %	Yield[c] PhPh, %	Yield of 1,[c,d] %
i-Pr$_2$NEt[e]	I	130	1	None	97	3	85
Bu$_3$N[e]	I	130	1	None	97	3	58
N(CH$_2$CH$_2$)$_3$N[f]	I	130	1	None	50	0	31
i-Pr$_2$NEt[e]	I	130	1	HMP	94	47	47
NaHCO$_3$	I	130	2	NMP	100	4	95[g]
NaOAc	I	140	7	HMP	75	3	23[h]
Et$_3$N	Br	130	2	DMF	81	0	Trace
Et$_3$N	Br	110	5	None	42	0	6
i-Pr$_2$NEt	Br	130	20	HMP	25	0	18
i-Pr$_2$NEt	Br	120	20	None	40	0	12
NaHCO$_3$	Br	130	2	DMF	100	0	100
NaHCO$_3$[i]	Br	130	2	DMF	100	0	84
Na$_2$CO$_3$	Br	130	10	DMF	91	0	73
Na$_2$CO$_3$[i]	Br	130	4	DMF	99	0	88
Na$_3$PO$_4$·12H$_2$O	Br	110	10	DMF	79	0	63
Na$_3$PO$_4$·12H$_2$O[i]	Br	110	10	DMF	77	0	54
MgCO$_3$	Br	140	10	DMF	33	0	20
MgCO$_3$[i]	Br	140	10	DMF	32	0	28
NaOAc	Br	130	6	DMF	24	0	10
NaOAc[i]	Br	130	6	DMF	37	0	14

[a] 50 mmol of C_6H_5X, 75 mmol of methallyl alcohol, 60 mmol of base, 0.45 mmol of PdOAc$_2$ and 20 ml of solvent under N$_2$. When X = Br, 0.9 mmol of PPh$_3$ added also. [b] Conversion of C_6H_5X by GC, internal standard. [c] Based on 100% conversion of C_6H_5X, GC internal standard. [d] Product identified by MS, NMR, C, H, analysis, bp 96° (10 mm) [lit.[5] 71–75° (3 mm)]. [e] 50 mmol of base. [f] 25 mmol of base. [g] 60% yield isolated in a similar experiment in HMP. [h] Isolated yield. [i] 0.1 g of Et$_3$N added.

ety of other conditions with diisopropylethylamine and other tertiary amines including diethylaniline, 2,6-lutidine, and 1,5-diazabicyclo[5.4.0]undec-5-ene, were unproductive.

A variety of inorganic bases were then tried for the bromobenzene reaction. Outstanding among these was sodium bicarbonate, which, in a polar aprotic solvent, gave the product rapidly in high yield. Further, the product was found to be stable to continued heating in the reaction mixture. Other carbonates were not as successful, especially the less soluble ones such as CaCO$_3$, which in 18 hr at 130° gave only a 20% conversion. If this is due to the insolubility of the carbonates, a small amount of a tertiary amine could catalyze their reaction. In agreement with this, it was found that a trace of triethylamine increased the initial rates of reaction by a factor of ~2 for all the inorganic bases except Na$_3$PO$_4$·12H$_2$O and NaOAc. The latter was found to have a detectable solubility in dimethylformamide while the solubility of the phosphate would be increased by the presence of the water of crystallization. Water in small amounts was also found to increase the rate of reaction when Na$_2$HPO$_4$ or Na$_2$CO$_3$ was used as base. The latter combination was as effective as Na$_2$CO$_3$ with a catalytic amount of triethylamine.

Since sodium bicarbonate decomposes at reaction temperatures, the mixture of Na$_2$CO$_3$ and H$_2$O which would be formed was compared with NaHCO$_3$. The latter was clearly superior, demonstrating that its effectiveness was inherent to sodium bicarbonate itself and not its decomposition products. The combination of Na$_2$CO$_3$ and H$_2$O gave a high initial rate which slowed greatly after attaining ~40% conversion in 30 min at 130°.

Catalyst deactivation could have many causes. For sodium acetate it is probably a result of the ability of the acetic acid produced to compete for Pd^0 and deactivate it by reaction 5.

$$\mathrm{HOAc} + \mathrm{Pd}^0 \rightleftharpoons \mathrm{HPdOAc} \tag{5}$$

Acetic acid is known to have a retarding effect on reaction 1.[1] Tertiary amine hydrohalides may also be sufficiently acidic to react with Pd^0 species. The formation of catalytically inactive palladium species, especially π-allyl complexes, is probably a factor with some of the stronger bases. In some cases, however, catalyst deactivation appeared to be related to the decomposition of organopalladium intermediates to the elemental metal. When X = I, red-brown catalytic intermediates were formed which were stable to the end of reaction in the absence of phosphines. When X = Br, and NaHCO$_3$ was used as base, reaction 4 occurred in the absence of triphenylphosphine. Without the stabilizing effect of phosphines, however, palladium began to precipitate at an earlier stage of the reaction and the rate slowed down, making it difficult to achieve 100% conversion. In the absence of phosphines, the reaction was also quite solvent sensitive. Thus, with NMP as solvent, conversion of bromobenzene was only 50% after 5 hr at 145° to give equal amounts of biphenyl and 1. In HMP at 145°, however, bromobenzene was 98% converted after 3 hr, 1 was isolated in 72% yield, and only a trace of biphenyl was formed. Thus, while triphenylphosphine appears to be necessary to reaction 1 when X = Br,[2,3] it is not essential for reaction 4.

In the presence of triphenylphosphine, variation of the solvent had less effect and 1 was consistently produced in high yield in a variety of solvents such as DMF, HMP, NMP, tetramethylurea (TMU), and dimethylacetamide (DMAC). At higher temperatures (>140°), catalyst deactivation by precipitation of palladium metal occurred and the reaction stopped at high conversion. This was particularly apparent with DMF. An important factor in the choice of solvent appears to be the solubility of sodium bicarbonate, since the reaction was also found to proceed in ethylene glycol, but not in diethylene glycol dimethyl ether unless 5% water was added. Protic solvents gave poorer yields of 1 than the polar aprotic solvents. Chlorobenzene has been reported to give only traces of product in reaction 1[3] and our work confirmed this for reaction 4.

The product aldehyde 1 has been synthesized earlier by the related palladium-catalyzed reaction between phenylmercuric chloride and methallyl alcohol.[5] Although only one product was reported, we also obtained 5% of an isomer which was separated and identified by NMR as dimethylphenylacetaldehyde. Apparently addition of phenylpallad-

Table II
Reaction of Iodobenzene and Bromobenzene with Allylic Alcohols[a]

					Products, %				
					3-Aryl carbonyl		2-Aryl carbonyl		
Registry no.	Alcohol	Time, hr	Halogen	Conversion, %	GC[b]	Yield, %	GC[b]	Yield, %	Other products GC[b]
107-18-6	$CH_2{=}CHCH_2OH$	2	I	100	81	23[c]	19	10[c]	
513-42-8	$CH_2{=}C(CH_3)CH_2OH$	4	I	100	95	95[d]	5		
	$CH_2{=}C(CH_3)CH_2OH$	4	Br	100	95	86[d]	5		
6117-91-5	$CH_3CH{=}CHCH_2OH$	1	I	100	69	69	31	24	
	$CH_3CH{=}CHCH_2OH$	1.5	Br	93	69	45[c]	31	21[c]	
598-32-3	$CH_2{=}CHCH(CH_3)OH$	2	I	100	100	89[d]			
	$CH_2{=}CHCH(CH_3)OH$	2	Br	100	70	e			Unknown[f] 30
1569-50-2	$CH_3CH{=}CHCH(CH_3)OH$	20	I	99	80	50[c]	20		
556-82-1	$(CH_3)_2C{=}CHCH_2OH$	10	I	77	36		16		Biphenyl 31 Unknown[g] 17
	$(CH_3)_2C{=}CHCH_2OH$	4	Br	27			19		Biphenyl 19 Unknown[g] 35
115-18-4	$CH_2{=}CHC(CH_3)_2OH$	12	I	53					$PhCH{=}CHC(CH_3)_2OH$[h]
	$CH_2{=}CHC(CH_3)_2OH$	4	Br	65					
110-64-5	$HOCH_2CH{=}CHCH_2OH$	0.5	I	95					3-Phenyl-2,3-dihydrofuran[h]
	$HOCH_2CH{=}CHCH_2OH$	2	Br	100					

[a] 50 mmol of halobenzene, 75 mmol of allylic alcohol, 60 mmol of $NaHCO_3$, 0.45 mmol of $PdCl_2$ in 20 ml of solvent (NMP at 130° for X = I and HMP at 140° for X = Br), 1.35 mmol of PPh_3 added when X = Br. [b] Product distribution from GC. [c] Isolated yield. [d] From GC, based on internal standard. [e] In a similar experiment in which 0.45 mmol of $(Ph_2PCH_2)_2$ was substituted for PPh_3, the yield was 80% (GC) and 63% isolated. [f] This compound was subsequently isolated and identified as (*E*)-4-phenyl-3-buten-2-ol.[13] [g] This compound was subsequently isolated and identified as 3-methyl-2-phenyl-3-buten-1-ol.[13] [h] See text.

Table III
NMR Spectra[a]

Registry no.	Compd	δ, multiplicity (no. of protons), coupling constant in hertz
93-53-8	2-Phenylpropanal	9.60 d (1) J = 1.5; 7.35 m (5); 3.65 qd (1) J = 7, 1.5; 1.4 d (3) J = 7
104-53-0	3-Phenylpropanal	9.70 t (1) J = 1; 7.25 s (5); 3.1–2.6 m (4)
3805-10-5	2-Methyl-2-phenylpropanal	9.50 s (1); 7.28 s (5); 1.40 s (6)
1528-39-8	3-Phenyl-2-pentanone	7.23 s (5); 3.47 t (1) J = 7; 1.97 s (3), 2.4–1.2 m (2), 0.8 t (3)
2439-44-3	3-Methyl-2-phenylbutanal	9.74 d (1) J = 3; 7.3 m (5); 3.5–3.1 m (1); 2.4–1.8 m (1), 1.04 d (3) J = 6; 0.75 d (3) J = 6
1009-62-7	3-Methyl-3-phenylbutanal	9.53 t (1) J = 3; 7.35 m (5); 2.67 d (2) J = 3; 1.43 s (6)
56718-06-0	3-Phenyl-2,3-dihydrofuran	7.20 s (5); 6.50 m (1); 5.00 m (1); 4.7–4.0 m (3)

[a] 60 MHz in CCl_4 with Me_4Si. Spectra of other compounds agreed with published spectra.[5]

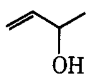
ium bromide to the double bond can occur in both senses.

Having established optimum conditions for reaction 4, the scope of the reaction was then investigated for a variety of other allylic alcohols.

2. Variation of the Allylic Alcohol. Using the optimum conditions found for the reaction of halobenzenes and methallyl alcohol, a wide variety of allylic alcohols were treated with iodo- and bromobenzene. Results are given in Table II. Where isolated yields were not obtained, the products were isolated by preparative GC and identified by NMR, ir, and MS. Where authentic samples were available, yields were sometimes obtained from GC data by the use of an internal standard. NMR data not previously reported[5] are given in Table III.

Although reactions of iodobenzene were conveniently fast at 130° with allyl alcohol and monosubstituted allylic alcohols, disubstitution severely retarded the rate. Reactions of bromobenzene at 145° in the presence of triphenylphosphine proceeded at least as easily as when using iodobenzene at 130°.

In the absence of triphenylphosphine, the reactions stopped after a partial conversion (i, 31% after 1 hr; ii, 25% after 1 hr; iii, 0% after 1.5 hr).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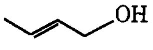
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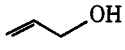
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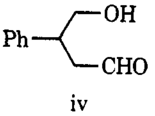
The reason for this is not yet clear, but it is likely that it is related to the precipitation of metallic palladium. Precipitation of palladium metal was almost immediate in the reaction of allyl alcohol and bromobenzene and no significant amount of products were formed. Running the reaction at lower temperatures did not help significantly. Even at 80°C, palladium metal was formed rapidly and the reaction was slow, resulting in deactivation of the catalyst at a very low conversion. Addition of triphenylphosphine helped to reactivate the catalyst in some of these cases.

Secondary reactions were important in the formation of the product from 2-butene-1,4-diol. The initial product was expected to be iv. This cyclized to the hemiacetal v, however, which dehydrated upon distillation to give the isolated product vi.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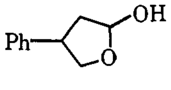
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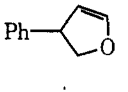
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Minor products (~5% or less) are not included in Table II. Where only one product is noted, the isomer resulting from the addition of the phenylpalladium species to the

Table IV
Reaction of Bromobenzene (50 mmol) with Allyl Alcohol (75 mmol)[a]

Time, hr	Conversion,[b] %	Yield[c] of $PhCH(CH_3)CHO$, %	Yield[c] of $PhCH_2CH_2CHO$, %
0.5	47	7	30
1.0	67	10	37
2.0	98	11	20
4.0	100	10	3

[a] With 60 mmol of $NaHCO_3$, 0.45 mmol of $PdCl_2$, and 1.35 mmol of PPh_3 in 20 ml of NMP under N_2 at 140°. [b] Conversion of C_6H_5Br by GC, internal standard. [c] Based on conversion by GC, internal standard.

Table V
Reaction of Halobenzene with Allyl Alcohol[a]

Halogen	Base	Solvent	Temp, °C	Time, min	Conversion[b] %	Yield,[c] % PhCH-(CH_3)CHO	PhCH$_2$-CH$_2$CHO
I	Et_3N	none	100	60	97	13	27
I	Et_3N	PhOPh	135	45	91	12	56
Br	$NaHCO_3$	HMP	110	240	90	13	12
Br	$NaHCO_3$[d]	HMP	110	120	87	9	22
Br	$NaHCO_3$[d]	NMP	100	60	51	4	6
Br	$NaHCO_3$[d]	NMP	130	10	46	6	23
Br[e]	$NaHCO_3$[d]	NMP	140	25	100	13	36
Br[e]	Na_2CO_3[d]	NMP	120	50	90	13	34

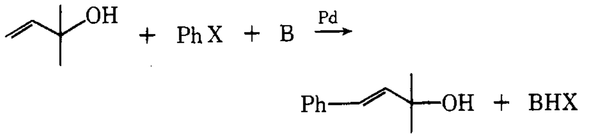
[a] 50 mmol of C_6H_5X, 75 mmol of allyl alcohol, 60 mmol of base, 0.45 mmol of $PdOAc_2$ and 20 ml of solvent. When X = Br, PPh_3 added, 0.9 mmol for first two cases and 1.35 mmol subsequently. [b] Conversion of C_6H_5X by GC, internal standard. [c] Based on 100% conversion (GC, internal standard). [d] A catalytic amount (0.2 g) of diisopropylethylamine added. [e] Allyl alcohol added gradually during reaction.

double bond in the reverse sense was not a significant product, although it may be formed. Where two major products were formed, the distribution did not appear to vary with the halogen used, the solvent, or the presence, amount, and nature of the phosphine. With the exception of methallyl alcohol, the only reactions which were optimized to any extent were those of allyl alcohol and 2-methyl-3-buten-2-ol, both of which suffered from competing side reactions.

3. Reaction of Halobenzenes with Allyl Alcohol. The product distribution from the reaction of allyl alcohol appeared to change with time in favor of 2-phenylpropanal. Aldehyde yields were therefore monitored continuously using an internal standard and the changing product distribution traced to a preferential destruction of 3-phenylpropanal (Table IV). Presumably this is due to a base-catalyzed aldol condensation.

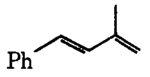
Table V shows that the destruction of 3-phenylpropanal can be minimized. For iodobenzene, a tertiary amine could be used and in this case a nonpolar solvent improved yields (tertiary amines are very poor aldol catalysts).[6] For bromobenzene an inorganic base was necessary with a polar aprotic solvent but a catalytic amount of a tertiary amine increased the rate and decreased aldehyde destruction. Generally these palladium-catalyzed reactions were best carried out at as low a temperature as possible to avoid catalyst and product decomposition. In the case of allyl alcohol, however, 3-phenylpropanal destruction was more pronounced at lower temperatures in the range 100–140°. Yields were further improved by adding the allyl alcohol gradually during the reaction so that its concentration (or that of the corresponding alkoxide) was minimized.

4. 2-Methyl-3-buten-2-ol. Reaction 6 was unaccountably slow with sodium bicarbonate and gave low yields for both X = I and X = Br.



(6)

With a tertiary amine, however, iodobenzene gave an 84% conversion in only 30 min at 120° (no solvent). The product consisted of the alcohol (90%) and the corresponding olefin vii (10%). As time increased, the ratio of olefin to alcohol increased, e.g., vii/viii = 4 at 2.5 hr and ∞ at 6 hr.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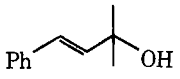
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This transformation was attributed to the catalytic effect of the amine hydroiodide or the small amount of acid in equilibrium with it. Although the amine gave a faster reaction than sodium bicarbonate, it had the disadvantage of causing the dehydration of the product. Fortunately it was possible to combine the advantages of amine and bicarbonate by using a catalytic amount of amine with the usual excess of sodium bicarbonate. In this case, a 90% conversion resulted after 30 min at 120° and the ratio of olefin to alcohol remained constant at 0.1 for 5.5 hr. The yield of alcohol was then determined by GC to be approximately 92% by the use of an internal standard.

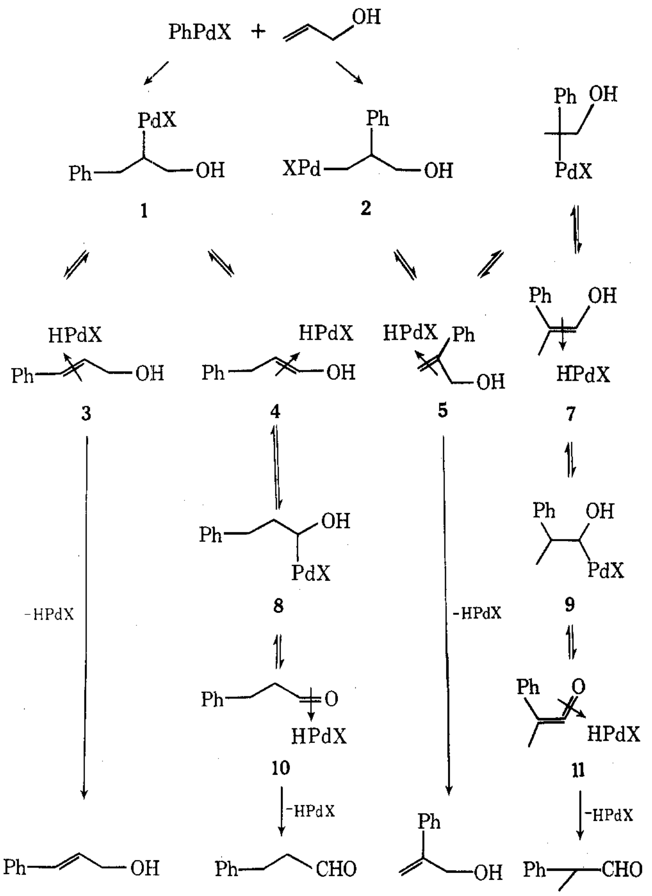
When the same combination of sodium bicarbonate with a catalytic amount of a tertiary amine was used for bromobenzene ($PPh_3/Pd = 2$), an 83% yield of the alcohol was obtained after 3 hr at 120° (solvent DMF).

Discussion

A common mechanism has been proposed for the arylation of olefins by phenylmercuric salts[7] and by aryl halides.[2,3] A comparison between the present work and the arylation of allyl alcohols by phenylmercuric salts[5] is therefore appropriate.

In both cases, arylpalladium halides are generated and these are expected to add to allyl alcohol to give intermediates **1** and **2** of Scheme I. These would be in equilibrium with intermediates **3**, **4**, and **5** which could give the free olefins by exchanging with other neutral ligands in solution. Since **5** is the enol form of 3-phenylpropanal, it would be

Scheme I



HPdX ⟶ Pd + HX
Pd + PhX ⟶ PhPdX

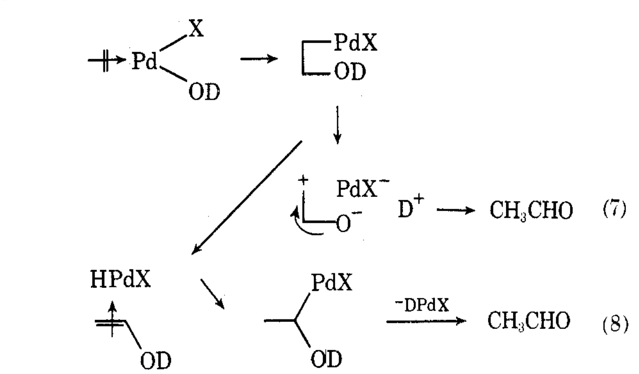
formed together with cinnamyl alcohol and 2-phenylallyl alcohol. If however, readdition of HPdX is fast compared to olefin exchange, intermediates **6–11** would also be formed. Of these, **10** and **11** would be aldehyde complexes which, being less stable than olefin complexes, would rapidly exchange and thereby favor formation of carbonyl products.

Two extreme cases may thus be distinguished: case A, in which coordinated olefins exchange rapidly and products are formed in a stepwise fashion (this favors the formation of unsaturated alcohols which could then slowly isomerize to carbonyl products); case B, in which a multistep olefin isomerization within the coordination sphere of the metal complex is faster than olefin exchange (in this case, carbonyl products would be favored).

Heck examined the reaction between phenylmercuric salts and allyl alcohol and found only 3-phenylpropanal, allylbenzene, and cinnamyl alcohol in the ratio 10:3:1. The last product suggests case A. However, in the reaction between crotyl alcohol and phenylmercuric salts, both the 2- and 3-phenylaldehydes were found, consistent with case B.

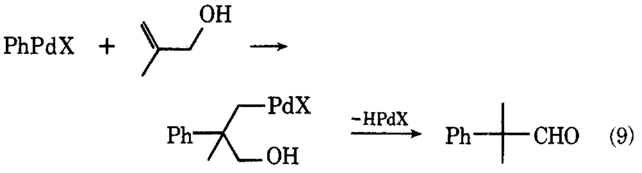
In our work the major products from allyl alcohol were 2- and 3-phenylpropanol, suggesting case B. In view of the differences found between allyl alcohol and crotyl alcohol in the earlier work, we also repeated the stoichiometric reaction between phenylmercuric acetate, palladium acetate, and allyl alcohol and found the dominant products to be biphenyl > 3-phenylpropanal > 2-phenylpropanal. The ratio of 3 to 2 addition was approximately 15. The large amount of biphenyl explains why phenylmercuric salts gave lower yields of aldehydes than the present synthesis.

Case B has been invoked in the past to explain results obtained in certain metal-catalyzed isomerizations.[8] One such result pertaining to the Wacker oxidation of ethylene to acetaldehyde is particularly relevant, since similar catalytic intermediates arise by a completely different reaction. Here, a stepwise mechanism involving the intermediacy of vinyl alcohol[9] was eliminated by the discovery that deuterium was not incorporated into the acetaldehyde when the reaction was carried out in D_2O.[10] Reaction 7 is the most commonly accepted explanation.[11] This involves the elimination of D^+ and PdX^- combined with a 1,2 hydride shift. A variant is reaction 8, in which the hydride shift is facilitated by palladium.



The latter mechanism was suggested by Heck[12] and led us to suggest the related mechanism (case B) for the present synthesis.

The reaction of methallyl alcohol with halobenzenes produced 5% of a product, 2-methyl-2-phenylpropanal, which cannot be explained by case B but requires a 1,3 hydride shift (reaction 9).



Palladium cannot facilitate this reaction via a π-olefin complex. Possible intermediates are a palladium π-cyclopropane intermediate or a cyclic palladium alkoxide.[13]

When this work was concluded we learned that Melpolder and Heck had been working along related lines and we are grateful to them for a copy of their paper prior to publication.[13] In common with us, they were unable to obtain stable products from aryl bromides and primary allylic alcohols when tertiary amines were used as bases. With the secondary alcohol, 3-buten-2-ol, they were more successful and obtained good yields of products. With this alcohol we found that sodium bicarbonate promoted a very much faster reaction than tertiary amines under our conditions. We attribute this difference to the products of the neutralization of the base. With tertiary amines, the amine hydrohalide which is formed probably dissociates to form the free acid in sufficient amount to partially deactivate the catalyst by reacting with it. Sodium acetate behaves similarly, since the catalyst is apparently basic enough to react with acetic acid. Sodium bicarbonate, however, has the virtue of liberating carbonic acid, which is expelled from the system as carbon dioxide.

(*E*)-4-Phenyl-3-buten-2-ol was a major product under the conditions used by Melpolder and Heck. This caused us to reexamine the corresponding reaction which we had run using sodium bicarbonate. Here we also found (*E*)-4-phenyl-3-buten-2-ol but in lesser amount. The ratio of products for 3 substitution was carbonyl/alcohol = 0.4 in our case vs. 0.8 in theirs. In the reactions of 3-methyl-2-buten-1-ol, unsaturated alcohols were also found as products and this additional information is noted in Table II. Case A products, therefore, appear to become significant with certain structures. However, case B products are favored under our conditions and we have obtained carbonyl compounds as major products from some unsaturated alcohols in which the double bond and hydroxyl function are well separated, e.g., 4-methyl-4-penten-1-ol. Even 1-decen-10-ol gave significant amounts of aldehyde products. We will report further on the reactions of nonallylic unsaturated alcohols in a subsequent paper.

Experimental Section

Reagents, catalysts, and solvents were commercial products and were used without purification.

Reactions were carried out under a nitrogen blanket in a flask equipped with a serum cap for the removal of GC samples. When conversion reached 100% or ceased, the reaction mixture was stirred with a five- to tenfold excess of water and extracted with toluene. The products were then distilled from the toluene extract or separated by preparative GC. In some cases, yields were obtained by GC during or at the end of the experiment, by the addition of an internal standard. A typical example follows. Deviations from this procedure are noted in the Results section.

3-Phenyl-2-methylpropanal. $PdCl_2$ (0.80 g) was dissolved in 200 ml of hexamethylphosphoramide at 140° and cooled, and 79 g of bromobenzene, 54 g of methallyl alcohol and 50 g of sodium bicarbonate added. The mixture was heated under nitrogen while stirring and monitored by GC. After 3 hr the reaction mixture was cooled, 200 ml of toluene was added, and the mixture was extracted twice with 1 l. of water. The toluene solution was then evaporated to give 63 g of liquid which was distilled under nitrogen at 10 mm pressure to give 53 g of 3-phenyl-2-methylpropanal (72% yield).

(1) Conversions and yields may frequently be improved by the addition of triphenylphosphine, e.g., 2.4 g (2 mol/mol $PdCl_2$).

(2) Rates may be increased by the addition of a small amount of a tertiary amine, e.g., 1 g of triethylamine.

(3) Satisfactory results have also been obtained in some cases when the concentration of the palladium catalyst was decreased by a factor of 0.2 and even 0.04.

Registry No.—Iodobenzene, 591-50-4; bromobenzene, 108-86-1; 3-phenylbutanal, 16251-77-7; 2-phenylbutanal, 2439-43-2; 3-phenyl-2-butanone, 769-59-5; 2-methyl-4-phenyl-3-buten-2-ol, 25625-21-2.

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Hydroboration of Monoterpene Alcohols

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The reaction of linalool (1) with excess borane in tetrahydrofuran at ambient temperature affords 3,7-dimethyl-2,6-octanediol (3) and 3,7-dimethyl-1,3,6-octanetriol (2), while treatment of 1 with 0.67 equiv of borane produces 3,7-dimethyl-1-octen-3,6-diol (8). Hydroboration of linalool (1) with disiamylborane yields 3,7-dimethyl-6-octen-1,3-diol (13). The reaction of geraniol (15) or citral (14) with borane in THF yields after oxidation a mixture of 2 and 3,7-dimethyl-1,2,6-octanetriol (18). Distillation of the intermediary boranes yields 22% of 8-isopropyl-5-methyl-1-bora-2-oxabicyclo[3.3.0]octane (16). The remainder of the organoboranes undergo β-elimination upon heating to afford, after oxidation, 3,7-dimethyl-1-octen-6-ol (20) and 3,7-dimethyl-1,6-octanediol (21).

Cornforth[1] has reported that the hydroboration–oxidation of linalool (1) results in the formation of 30% of an unidentified diol in addition to 60% of 3,7-dimethyl-1,3,6-octanetriol (2), even when an excess of borane is used. We have confirmed these observations using a 50% excess of borane in THF and find that the diol is a 4:1 mixture of 3,7-dimethyl-2,6-octanediol (3) and 3,7-dimethyl-3,6-octanediol (4). Jones oxidation of the diol mixture afforded 3,7-dimethyl-2,6-octanedione (5) and 4-methyl-4-hydroxyhexanoic acid lactone (6).[2]

In order to gain an insight into the formation of diols 3 and 4, linalool (1) was treated with 0.67 equiv of borane. Oxidation afforded recovered linalool (28%), triol 2 (9%), and 34% of 3,7-dimethyl-1-octene-3,6-diol (8) which was converted to the known monoacetate 9[3] using acetic anhydride and pyridine. The formation of the 3,6-diol 8 to the exclusion of the 1,3-diol 13 is most likely the result of ini-