Organophosphinepalladium Complexes as Catalysts for Vinylic Hydrogen Substitution Reactions

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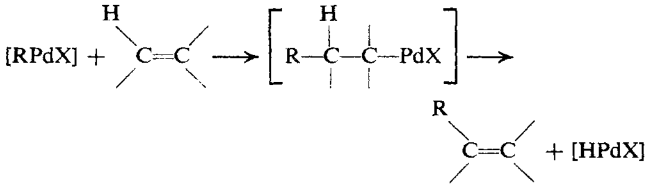
Abstract: Aryl and vinylic bromides and iodides react at 100–135° with olefins in the presence of a tertiary amine and a catalyst composed of palladium acetate and 2 equiv of triphenylphosphine. New olefins are formed in which a vinylic hydrogen in the original olefin has been replaced by the organic group of the halide. The reaction is stereospecific to the extent of about 70% with *cis*- and *trans*-1-phenyl-1-propene.

We have previously reported palladium metal formed *in situ* from palladium acetate catalyzed the vinylic hydrogen substitution reaction of olefins with aryl iodides, benzyl chloride, and β-bromostyrene in the presence of a tertiary amine.[1] While this reaction in most respects was a significant improvement over the earlier version which employed organomercury compounds rather than organic halides,[2] it still had two major problems. The most serious of these was that the reaction was limited to the often difficultly obtainable aryl iodides and as we now know to vinylic iodides with the exception of the bromostyrenes which reacted rather slowly. The second problem was that there was an essentially complete loss of stereochemistry when pure cis or trans olefins were reacted. The research reported herein was undertaken with the objective of overcoming these deficiencies. Significant progress has been made and the results are now reported since the new modification will make these unique reactions more useful than they were previously.

$$\mathrm{RX} + \mathrm{Pd} \rightleftharpoons [\mathrm{RPdX}]$$



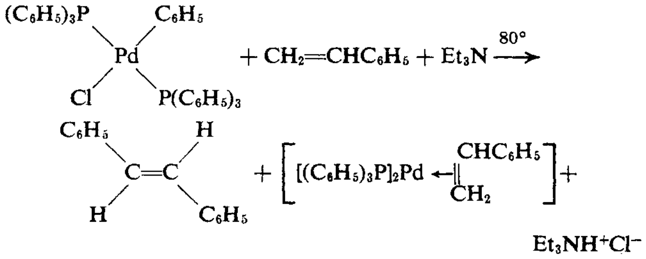
$$[\mathrm{HPdX}] + \mathrm{R_3'N} \longrightarrow \mathrm{Pd} + \mathrm{R_3'NH^+X^-}$$

Results and Discussion

Oxidative additions of a wide variety of aryl, alkyl, and vinyl halides to tetrakistriphenylphosphinepalladium(0) have been carried out.[3-5] These additions occurred readily even with aryl bromides in contrast to the lack of reactivity of palladium metal with aryl bromides in our catalytic reactions. It appeared therefore that the phosphine complex might be a more reactive catalyst for the vinylic substitution. Experiments confirmed this. Aryl iodides reacted more easily and aryl bromides reacted reasonably well when triphenylphosphine and palladium acetate were employed as the catalyst instead of palladium acetate alone. Vinylic iodides reacted without the phosphine but more rapidly with it. Vinylic bromides such as 2-bromopropene required the phosphine catalyst. We are still investigating the vinylic halide reactions and more details will be reported in a future publication.

A variety of organophosphines, phosphites, arsines, and amines were tested and triphenylphosphine was found to be about the most useful ligand. The optimum ratio of triphenylphosphine to palladium acetate for the bromobenzene–methyl acrylate reaction was about 2:1. Ratios of 4, 3, and 1:1 gave slower reaction rates but similar yields of methyl cinnamate.

Even though chlorobenzene oxidatively adds to tetrakistriphenylphosphinepalladium(0) at 135°[5] we were unable to obtain more than very low yields of vinylic substitution products with it under a wide variety of conditions. The chlorobenzene remained unreacted. Preformed *trans*-chlorobistriphenylphosphinepalladium(0), however, does react with olefins such as styrene with an amine present at 80° to form the expected vinylic substitution products in good yields.[6] Yields are less than 50% in the absence of amine, however.



The reactions carried out catalytically are listed in Table I. A variety of aryl bromides was found to react. In general electron-withdrawing substituents increased the reactivity of the bromides. *p*-Bromoanisole required temperatures of 135° in order to react at an appreciable rate while, for example, methyl *p*-bromobenzoate reacted easily and more rapidly at 100°. The relatively hindered 2-bromobiphenyl also reacted slowly and gave only 36.5% of product with methyl acrylate after 65 hr at 135°. In this example significant hydrolysis occurred during the reaction under dry nitrogen even though all reagents were carefully dried. A side product formed in this reaction was biphenyl (identified by nmr and vpc). The reducing agent responsible has not been identified.

The reaction of bromobenzene or iodobenzene with 1-hexene gave a mixture of at least four significant isomeric products. Judging by vpc retention times they

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(1) R. F. Heck and J. P. Nolley, Jr., *J. Org. Chem.*, 37, 2320 (1972).

(2) R. F. Heck, *J. Amer. Chem. Soc.*, 93, 6896 (1971).

(3) P. Fitton and E. A. Rick, *J. Organometal. Chem.*, 28, 287 (1971).

(4) P. Fitton, M. P. Johnson, and J. E. McKeon, *Chem. Commun.*, 6 (1968).

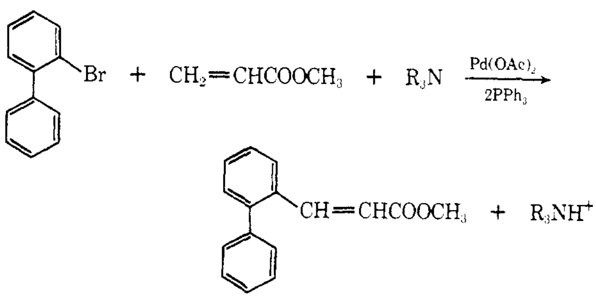
(5) D. R. Coulson, *Chem. Commun.*, 1530 (1968).

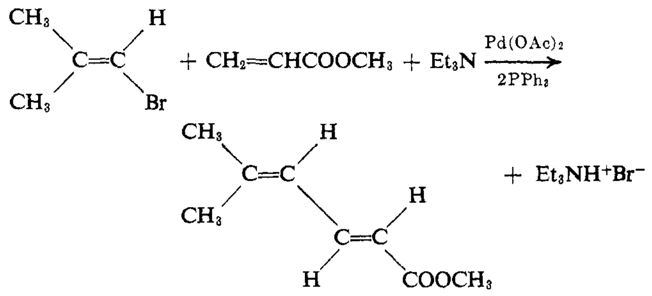
(6) Unpublished work of K. K. Chow.

Table I. Olefinic Substitution Reactions with Organic Halides[a]

Organic halide	Olefinic compd	Base	Reaction temp, °C	Reaction time, hr	Products (% yield)	Mp of product, °C (reported)
Bromobenzene	Methyl acrylate	TMED[b]	125	28	*trans*-Methyl cinnamate (85)[c]	
Bromobenzene	1-Hexene	Et_3N	100[j]	41	1-Phenyl-1-hexene (44.2)[c] Other phenylhexenes (42.6)[c]	
Iodobenzene	1-Hexene	Et_3N	100[j]	22	1-Phenyl-1-hexene (41.8)[c] Other phenylhexenes (39.6)	
Iodobenzene[k]	1-Hexene	Et_3N	100[j]	55.5	1-Phenyl-1-hexene (27.9)[c] Other phenylhexenes (37.1)	
p-Bromoanisole	Methyl acrylate	TMED[b]	135	36	*trans*-Methyl *p*-methoxycinnamate (54)	88.0–89.5 (90)[d]
Methyl *p*-bromobenzoate	Methyl acrylate	N-Bu_3N	100	7	*trans*-Methyl *p*-carbomethoxycinnamate (81)	125–126 (125.5–126.5)[e]
Methyl *p*-bromobenzoate	Styrene	N-Bu_3N	100	8	*trans*-4-Carbomethoxystilbene (77.5)	159–160 (158–159)[f]
p-Nitrobromobenzene	Methyl acrylate	N-Bu_3N	100	7	*trans*-Methyl *p*-nitrocinnamate (73)	160–161 (161°)[d]
p-Chlorobromobenzene	Methyl acrylate	N-Bu_3N	100	12	*trans*-Mèthyl *p*-chlorocinnamate (54)	75–76 (76–76.5°)[g]
2-Bromobiphenyl	Methyl acrylate	TMED[b]	135	65	*trans*-*o*-Phenylcinnamic acid (36.5)[h]	200–201 (202)[i]
2-Methyl-1-bromo-1-propene	Methyl acrylate	Et_3N	100[j]	70	*trans*-Methyl 5-methyl-2,4-hexadienoate (75)	Bp 90 (13 mm)

[a] Reactions were catalyzed by 1–2 mol % of 1:2, $Pd(OAc)_2:PPh_3$. No solvent was used. Product identities were confirmed by vpc and nmr analyses. [b] TMED = tetramethylethylenediamine. [c] Yield determined by gas chromatography. [d] I. Heilbron, "Dictionary of Organic Compounds," Vol. IV, Oxford University Press, New York, N. Y., 1955. [e] R. F. Heck, *J. Amer. Chem. Soc.*, **90,** 5518 (1968). [f] R. C. Fuson and H. G. Cooke, Jr., *J. Amer. Chem. Soc.*, **62,** 1180 (1940). [g] C. S. Rondestvedt, Jr., and C. D. Ver Nooy, *ibid.*, **77,** 4878 (1955). [h] Obtained by hydrolysis of crude reaction product. [i] S. H. Zaheer and S. A. Faseeh, *J. Indian Chem. Soc.*, **21,** 381 (1944). [j] Reaction carried out in a capped tube. [k] No PPh_3 used.





were the same products as were obtained previously in the reaction of phenylmercuric acetate with palladium acetate and 1-hexene.[2] The triphenylphosphine ligands increased the yield of 1-phenyl-1-hexene (identified by nmr) from about 28 to 42% in the reaction with iodobenzene.

Various tertiary amines have been employed in these reactions and relatively little difference between them has been noted. Some difficulty in removing tributylamine salts from organic solvents by water washing was encountered. Tetramethylethylenediamine and triethylamine gave reaction mixtures which were easier to purify since the amine salts were more water soluble. The olefins which were reacted included methyl acrylate, styrene, 1-hexene, and 1-phenyl-1-propene suggesting that this reaction is applicable to a wide range of mono- and disubstituted olefinic compounds.

The vinylic bromide, 2-methyl-1-bromo-1-propene, reacted with methyl acrylate at 100° to form in 75% yield *trans*-methyl 5-methyl-2,4-hexadienoate. This appears to be a general reaction of vinyl iodides and bromides and other examples are currently being studied.

Table II lists the results of the reactions of various phenylpalladium reagents with *cis*- and *trans*-1-phenyl-1-propene and with 2-phenyl-1-propene. Previously it was shown that phenylmercuric acetate with a stoichiometric amount of palladium acetate reacted with *cis*- or *trans*-1-phenyl-1-propene at 30° to give 88% or more of the isomeric 1,2-diphenyl-1-propene expected from cis addition of the phenylpalladium complex followed by a cis elimination of a hydridopalladium complex.[7] The same reaction at 100° with iodobenzene and a catalytic amount of palladium acetate, however, showed very little stereospecificity.[1] We have repeated this reaction and obtained a much higher yield with a longer reaction time. Previously we had incorrectly identified one of the products from the phenylation of *trans*-1-phenyl-1-propene as *cis*-1,2-diphenyl-1-propene while it actually was 1,1-diphenyl-1-propene. Inclusion of 2 equiv of triphenylphosphine per mole of palladium acetate catalyst significantly improved the specificity of the two reactions at 100°. The reactions of either iodo- or bromobenzene with *cis*- or *trans*-1-phenyl-1-propene now gave about 70% of the cis addition–cis elimination product. The remainder of the product was a mixture of the opposite isomer, 1,1-diphenyl-1-propene and 1,2-diphenyl-2-propene. Thus, the phosphinepalladium catalyst is useful for stereospecific syntheses. The specificity of the reaction is not improved by the use of various other ligands in place of triphenylphosphine. We have tried triphenyl phosphite, tri-*n*-butylphosphine, trimethylolpropane phosphite, triphenylarsine, *o*-phenanthroline, and tetramethylethylenediamine (without triphenylphosphine) and the reactions were less specific and much slower than with triphenylphosphine. Similarly inclusion of various different bases and solvents did not

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(7) R. F. Heck, *J. Amer. Chem. Soc.*, **91,** 6707 (1969).

Table II. Reactions of Phenylpropenes with Phenylpalladium Complexes

Phenylating agent	Phenylpropene	Catalyst	Base or solvent	Reaction temp, °C	Reaction time, hr	Total yield %	Products (% yield)[c] *cis*-1,2-Diphenyl-1-propene	*trans*-1,2-Diphenyl-1-propene	2,3-Diphenyl-1-propene	1,1-Diphenyl-1-propene
C_6H_5HgOAc[a]	*cis*-1-Phenyl-1-propene	$Pd(OAc)_2$ (stoichiometric)	CH_3CN	30	2	99	88.5	4.0	7.5	0
C_6H_5I	*cis*-1-Phenyl-1-propene	$Pd(OAc)_2$	Et_3N	100	34	85	13.5	57.0	22.0	6.9
C_6H_5I	*cis*-1-Phenyl-1-propene	$Pd(OAc)_2 + 2PPh_3$	Et_3N	60	142	80	79.6	14.6	0	5.8
C_6H_5I[b]	*cis*-1-Phenyl-1-propene	$Pd(OAc)_2 + 2PPh_3$	Et_3N	100	34	93	75.8	15.2	1.7	7.3
C_6H_5Br	*cis*-1-Phenyl-1-propene	$Pd(OAc)_2 + 2PPh_3$	Et_3N	100	82	92	73.4	19.2	0	7.4
C_6H_5HgOAc[a]	*trans*-1-Phenyl-1-propene	$Pd(OAc)_2$ (stoichiometric)	CH_3CN	30	2	86	0	99.5	0.5	0
C_6H_5I	*trans*-1-Phenyl-1-propene	$Pd(OAc)_2$	Et_3N	100	34	83	2.0	52.7	13.6	31.7
C_6H_5I	*trans*-1-Phenyl-1-propene	$Pd(OAc)_2 + 2PPh_3$	Et_3N	100	34	99	0	71.0	0	29.0
C_6H_5Br	*trans*-1-Phenyl-1-propene	$Pd(OAc)_2 + 2PPh_3$	Et_3N	100	43	72	0	78.5	0	21.5
C_6H_5HgOAc[a]	2-Phenyl-1-propene	$Pd(OAc)_2$ (stoichiometric)	CH_3CN	30	2	73	0	42.0	58.0	0
C_6H_5I	2-Phenyl-1-propene	$Pd(OAc)_2$	Et_3N	100	33	78	7.8	68.0	24.2	0
C_6H_5I	2-Phenyl-1-propene	$Pd(OAc)_2 + 2PPh_3$	Et_3N	100	33	79	5.3	88.0	6.7	0
C_6H_5Br	2-Phenyl-1-propene	$Pd(OAc)_2 + 2PPh_3$	Et_3N	100	33	66	4.4	87.8	7.8	0

[a] Data taken from ref 7. [b] At 84% reaction 18% of the unreacted 1-phenyl-1-propene was the trans isomer. [c] Products were identified as described in ref 7.

benefit the reaction. The use of tri-*p*-anisyl- or tri-*o*-tolylphosphine in place of triphenylphosphine also gave essentially the same mixture of products at slightly faster rates.

Some conclusions can be drawn from the data in Table II. Clearly the direction of addition of the phenylpalladium complex is very little influenced by the presence of the triphenylphosphine ligands since in the iodobenzene reactions about the same yields of 1,1-diphenyl-1-propene are obtained from *cis*- and from *trans*-1-phenyl-1-propene whether or not triphenylphosphine is present. The triphenylphosphine, however, does markedly influence the amount of elimination of the allylic hydrogen that occurs forming 2,3-diphenyl-1-propene. Essentially none of this product is formed in the presence of the phosphine. The same effect probably accounts for the similar increase in the conjugated olefin formed in the phenylation of 1-hexene with the phosphine catalyst as shown in Table I. On the other hand, 2-phenyl-1-propene still forms about 6.7% 2,3-diphenyl-1-propene even with the phosphine catalyst. Without the phosphine 24.2% was found. These facts are consistent with the triphenylphosphine influencing both the direction of the β-hydride elimination which likely occurs in these reactions and the internal rearrangement of palladium from one carbon to another by way of hydridopalladium–olefin complexes. The data are consistent with the equations shown in Scheme I. The triphenylphosphine appears to greatly reduce the amount of internal palladium hydride readdition to the point where the yield of 2,3-diphenyl-1-propene becomes less than about 2% where it is not accurately measurable.

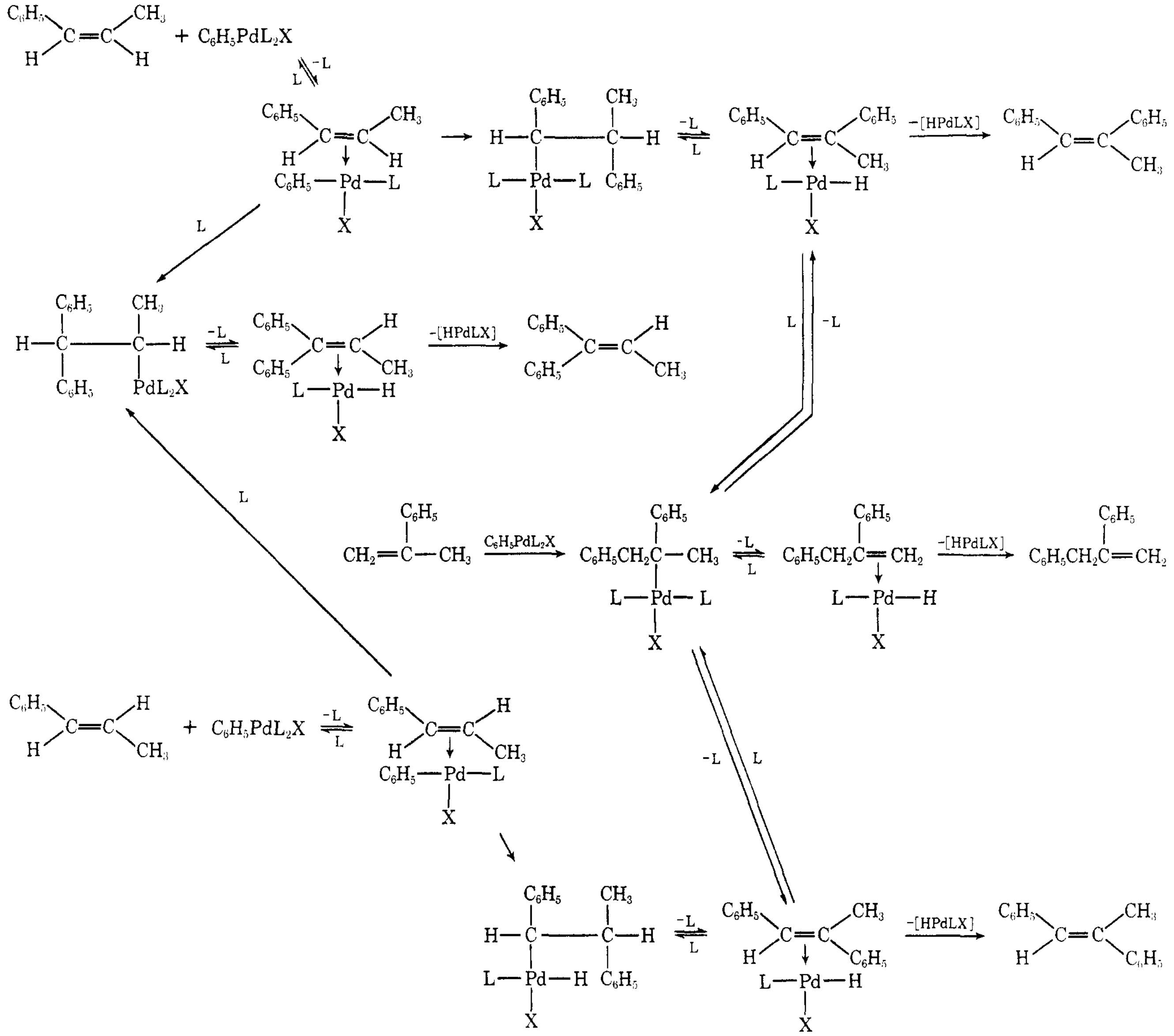
The reaction products mixtures were stable for many hours longer than required for complete reaction. However, some of the starting olefin in the case of *cis*-1-phenyl-1-propene was isomerized during the reaction to the trans isomer. In the reaction of iodobenzene with the cis olefin about 18% of the *remaining* olefin after the reaction was 84% complete had isomerized. Therefore some of the *trans*-1,2-diphenyl-1-propene and the 1,1-diphenyl-1-propene formed in this reaction is arising from rearranged olefin. This does not appear to be the only way these isomers are formed, however, since even at only 19% reaction the product contained 8.5% *trans*-1,2-diphenyl-1-propene and we knew from previous work[7] that the *trans*-1-phenyl-1-propene was not much different in its reactivity in the phenylation than the cis isomer.

A rough measure of the half-lives of the reactions in Table II at 100° was made by observing products at various times during the course of the reactions. The results indicate that the 2 equiv of triphenylphosphine increase the rate of reaction of iodobenzene by a factor of only about 2 while the factor appears to be considerably larger with bromobenzene since very little product is obtained in the absence of triphenylphosphine even at elevated temperatures over a long period of time. With the phosphine catalyst iodobenzene was approximately four times more reactive than bromobenzene.

Experimental Section

General Procedure for Olefin Arylation with Aryl Bromides. A mixture of 20 mmol of aryl bromide, 25 mmol of olefin (40 mmol was used in the methyl cinnamate, methyl *p*-methoxycinnamate, and *o*-phenylcinnamic acid examples), 25 mmol of tri-*n*-butylamine,

Scheme I



triethylamine, or 20 mmol of tetramethylethylenediamine, 0.2 mmol of palladium acetate (Engelhard Industries), and 0.4 mmol of triphenylphosphine (twice as much catalyst was used in the *o*-phenylcinnamic acid preparation) were heated under a reflux condenser in an Argon atmosphere at the temperatures indicated (oil bath temperatures) in Table I or II until the aryl bromide had all reacted as determined by vpc. The reactions with triethylamine were carried out in capped tubes. Yields were determined by adding naphthalene as an internal standard and diluting the partially solid reaction mixtures with methylene chloride or by isolation. Solid products were isolated by diluting the reaction mixtures with 200 ml of 10% hydrochloric acid with stirring to dissolve the salts and excess amine. The insoluble material was separated by decanting or filtering and then extracted with several portions of hot hexane or heptane until no more could be extracted. The extracts were treated with decolorizing carbon, filtered, concentrated, and allowed to cool. The products generally crystallized from these solutions in a pure form. In the case of the reaction of 2-bromobiphenyl with methyl acrylate, however, the product was a mixture of the cinnamate ester and the cinnamic acid. The mixture was hydrolyzed with 4 g of sodium hydroxide in 75 ml of water and 75 ml of methanol by boiling for 48 hr. After dilution with 200 ml of water, extraction with ether (extracts contained 17% biphenyl), and acidification, the acid was extracted with methylene chloride. After drying, the solvent was evaporated and the acid was crystallized from ethanol.

1-Bromo-2-methyl-1-propene. A solution of 11.6 g (0.21 mol) of potassium hydroxide in 42 ml of ethylene glycol was stirred in a 250-ml three-necked flask at 140° while 20 g (0.093 mol) of 1,2-dibromo-2-methylpropene was added dropwise from a dropping funnel. The product distilled (bp ~75–85°) from the reaction mixture through the third neck of the flask as it was formed. The product was condensed, cooled in Dry Ice, and decanted from a small amount of ice from some water which also distilled. There was obtained 10.6 g (86%) of colorless product which appeared to be pure by vpc and nmr.

Methyl 5-Methyl-2,4-hexadienoate. A mixture of 2.70 g (20 mmol) of 1-bromo-2-methyl-1-propene, 2.14 g (25 mmol) of methyl acrylate, 2.52 g (25 mmol) of triethylamine, 0.045 g (0.2 mmol) of palladium acetate, and 0.104 g (0.4 mmol) of triphenylphosphine was heated in a capped heavy-walled Pyrex tube flushed with argon in a steam bath for 37 hr. After cooling the partially solid reaction mixture was extracted with four 50-ml portions of pentane. The extracts were distilled. There was obtained 0.84 g (30%) of product, bp 90° (13 mm). In a second experiment using naphthalene as an internal standard the yield of product by vpc increased to 75% after heating 70 hr at 100°. The distilled product gave a molecular weight of 140.0830 (calcd, 140.0837) by mass spectroscopy. The nmr spectrum in deuteriochloroform had bands at τ 8.10 (broad singlet, 6 protons), 6.33 (singlet, 3 protons), 4.33 (doublet, J = 15 Hz, one proton), 4.06 (doublet, one proton, J = 10.5 Hz), and 2.55 (double doublet, one proton). The product had infrared absorptions at 1709, 1609, and 1634 cm^{-1} as reported.[8]

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(8) L. Crombie and K. Mackenzie, *J. Chem. Soc.*, 4417 (1958).