76252-00-1; 3-bromo-2-propen-1-ol, 37675-33-5; (*E*)-3-bromo-2-methylpropenal dimethyl acetal, 76232-48-9; 2,3-dibromo-2-methylpropanal dimethyl acetal, 76252-01-2; (*Z*)-3-bromo-2-methylpropenal dimethyl acetal, 76252-02-3; 3-chloro-2-butanone, 4091-39-8; ethylene glycol, 107-21-1; 3-chloro-2-butanone ethylene ketal, 40609-93-6; 2-methyl-2,4-hexadienal dimethyl acetal, 76252-03-4; (*Z,E*)-2-methyl-2,4-hexadienal, 54716-14-2; 3-methyl-2,4-hexadienal dimethyl acetal, 76252-04-5; 3-methyl-2,4-hexadienal, 59502-64-6.

Supplementary Material Available: Table III containing the physical properties, NMR spectral data, and molecular weights of the products prepared (9 pages). Ordering formation is given on any current masthead page.

Palladium-Catalyzed Synthesis of 2,4-Dienoic Acid Derivatives from Vinylic Halides

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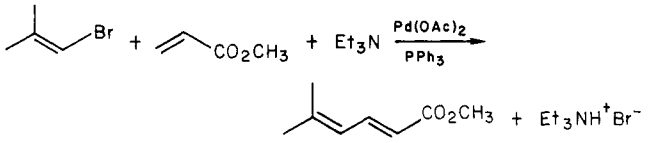
Received September 17, 1980

A wide variety of vinylic bromides and iodides have been coupled with acrylic, methacrylic, crotonic, and maleic esters and in some cases with the free acids, nitriles, and amides. In general, good yields of the 2,4-dienoic acid derivatives were obtained. The stereochemistry of the products was determined and the factors influencing the stereoselectivity of the reaction were studied.

Esters of 2,4-dienoic acids have been shown to be easily formed by the palladium-catalyzed reaction of 1-iodo- and 1-bromo-1-hexene, 1-bromo-2-methyl-1-propene, and methyl 3-bromo-2-methylacrylate with methyl acrylate in the presence of triethylamine.[1] Vinyl iodide and 2-

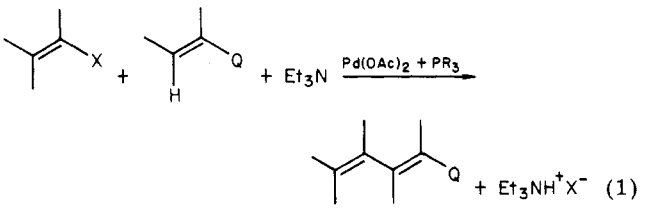


bromopropene in the reaction gave only Diels–Alder adducts of the dienoate products with methyl acrylate. Since the general reaction could be of significant synthetic value, we have investigated it in more detail with respect to the influence of substituents in the reactants on the rates, yields, and the stereochemistry of the products. We have also included examples of reactions of acrylonitrile, acrylamide, and methacrylamide which were not investigated previously.

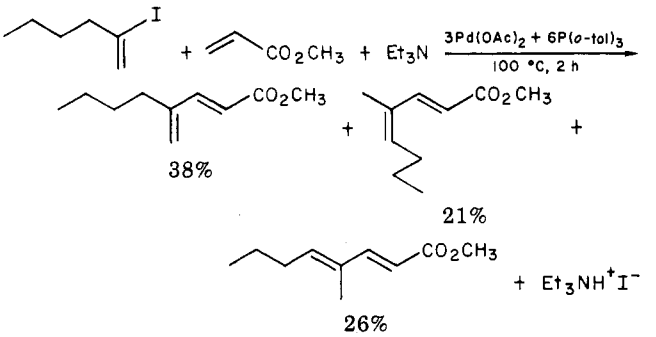
Results and Discussion

A variety of vinylic halides were allowed to react with acrylic acid, methyl acrylate, acrylonitrile, acrylamide, (*E*)-crotonic acid, (*E*)-methyl crotonate, methyl methacrylate, and methacrylamide in the presence of triethylamine and (usually) a palladium acetate–tri-*o*-tolylphosphine catalyst. The *o*-tolyl catalyst usually gives higher reaction rates than a triphenylphosphine catalyst. The results are summarized in Table I. The reactions carried out are listed with the unsaturated acids first, followed by esters, nitriles, and amides. Within each of these groups reactants are arranged in order of increasing numbers of carbon atoms present. Esters were used most frequently because of their availability and the ease of analysis of their reaction products by GLC.

In general, the reactions proceeded as found in our previous work to give good yields of conjugated dienoic acids or their derivatives according to eq 1. Exceptions



to this general reaction occurred with the least hindered reactants, (*E*)-2-bromo-2-butene, 2-bromo-1-hexene, and 1-bromocyclohexene, in their reactions with methyl acrylate, where major or exclusive products were Diels–Alder adducts of the expected dienoate esters with methyl acrylate. Rearranged dienoate esters were major products in the reaction of 2-iodo-1-hexene with methyl acrylate.



Reactivity. The rates of the reactions generally decrease as the number and/or the size of the alkyl substituents on either of the double bonds of the reactants increase. The electron-withdrawing carbomethoxyl group in (*E*)-methyl 3-bromo-2-methylpropenoate, on the other hand, significantly increases the reactivity of the halide in the reaction relative to 1-bromo-1-propene. Unfortunately, 3-bromoacrylic acid and its esters, nitrile, or amides cannot be used in this reaction, presumably because of facile dehydrohalogenation and polymerization of the resulting acetylene under the reaction conditions.

Acrylic acid and its ester and amide all have a similar reactivity but acrylonitrile is less reactive. Methyl methacrylate and methacrylamide are much less reactive than

(1) H. A. Dieck and R. F. Heck, *J. Org. Chem.*, **40**, 1083 (1975).

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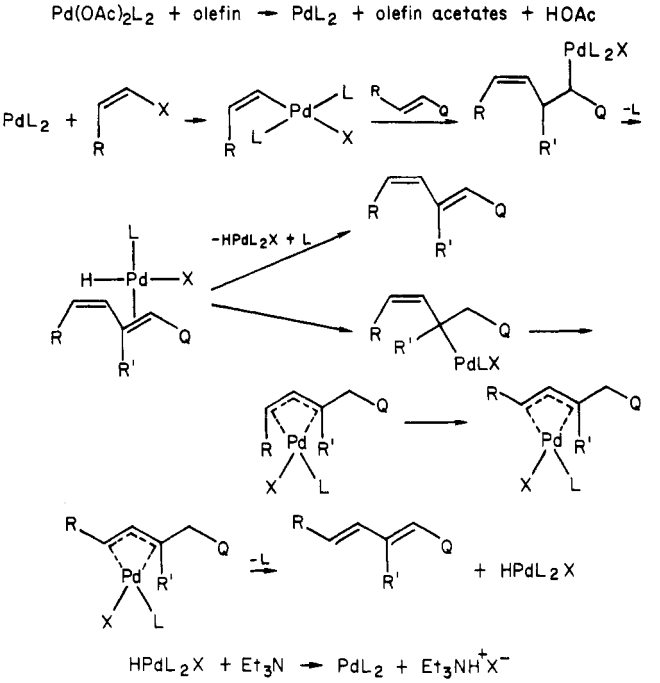
Table I. Palladium-Catalyzed Syntheses of 2,4-Dienoic Acid Derivatives

unsaturated[a] acid derivative	vinylic halide	amine, $\frac{Et_3N}{RX}$, molar ratio	catalyst,[b] $\frac{P(o\text{-tol})_3}{Pd(OAc)_2}$	temp, °C	time, h	product (% yield of isolated products)[i]
CH_2=$CHCO_2H$	$(CH_3)_2C$=$C(Br)CH_3$	3.00	2/1	125	43	(*Z*)-$(CH_3)_2C$=$C(CH_3)CH$=$CHCO_2H$ (85)
CH_2=$CHCO_2CH_3$	(*E*)-CH_3CH=$C(Br)CH_3$	3.00	6/3	125	24	CH_3CH=$C(CH_3)CH$=$CHCO_2CH_3$ (*E,E*, 29; *E,Z*, 8), Diels-Alder products (61)[c]
	(*E*)-$CH_3O_2CC(CH_3)$=$CHBr$	3.00	2/1	100	2	(*E,E*)-$CH_3O_2CC(CH_3)$=$CHCH$=$CHCO_2CH_3$ (80)
	(*Z*)-$CH_3(CH_2)_3CH$=$CHBr$	3.00	$\frac{PPh_3}{Pd(OAc)_2}=\frac{2}{1}$	125	96	$CH_3(CH_2)_3CH$=$CHCH$=$CHCO_2CH_3$ (*E,Z*, 51; *E,E*, 35; *Z,Z*, 3 (?))
		3.00	$\frac{PPh_3}{Pd(OAc)_2}=\frac{6}{3}$	125	2.5	$CH_3(CH_2)_3CH$=$CHCH$=$CHCO_2CH_3$ (*E,Z*, 76; *E,E*, 4; *Z,Z*, ~5 (?))
	(*Z*)-$CH_3(CH_2)_2C(CH_3)$=$CHBr$	3.00	2/1	125	6 days	(*E,Z*)-$CH_3(CH_2)_2C(CH_3)$=$CHCH$=$CHCO_2CH_3$ (79)
	(*E*)-$CH_3(CH_2)_2C(CH_3)$=$CHBr$	3.00	2/1	125	6 days	(*E,E*)-$CH_3(CH_3)_2C(CH_3)$=$CHCH$=$CHCO_2CH_3$ (79)
	$CH_3(CH_2)_3C(Br)$=CH_2	3.00	2/1	125	20	Diels-Alder products[c]
		3.00	6/3	100	72	Diels-Alder products[c]
	$CH_3(CH_2)_3C(I)$=CH_2	3.00	6/3	100	2	$CH_3(CH_2)_2CH$=$C(CH_3)CH$=$CHCO_2CH_3$ (*E,E*, 26; *E,Z*, 21); $CH_3(CH_2)_3C$(=CH_2)CH=$CHCO_2CH_3$ (38)
	(*Z*)-C_2H_5CH=$C(I)C_2H_5$	3.00	2/1	100	4	(*E,Z*)-C_2H_5CH=$C(C_2H_5)CH$=$CHCO_2CH_3$ (86)
	(*E*)-C_2H_5CH=$C(I)C_2H_5$	3.00	2/1	100	4	(*E,E*)-C_2H_5CH=$C(C_2H_5)CH$=$CHCO_2CH_3$ (85)
	(*E*)-$(CH_3O)_2CHC(CH_3)$=$CHBr$	3.00	8/2	100	20	(*E,E*)-$(CH_3O)_2CHC(CH_3)$=$CHCH$=$CHCO_2CH_3$ (90)
CH_2=$CHCO_2CH_3$	1-bromocyclohexene	3.00	2/1	100	15	(*E*)-methyl β-(1-cyclohexenyl)acrylate (38), Diels-Alder products[c]
	$BrCH$=$CHCH_2OTHP$[d]	2.00	$\frac{PPh_3}{Pd(OAc)_2}=\frac{2}{1}$	100	20	(*E,E*)-$THPOCH_2CH$=$CHCH$=$CHCO_2CH_3$ (50)
CH_2=$CHCN$	(*Z*)-C_2H_5CH=$C(I)C_2H_5$	3.00	6/1	100	24	C_2H_5CH=$C(C_2H_5)CH$=$CHCN$ (*E,Z*, 86; *Z,Z*, 2)
	(*Z*)-C_2H_5CH=$C(Br)C_2H_5$	3.00	6/3	125	96	C_2H_5CH=$C(C_2H_5)CH$=$CHCN$ (*E,Z*, 40; *Z,Z*, 10), $(C_2H_5)_2NCH_2CH_2CN$ (20)[e]
CH_2=$CHCONH_2$[f]	(*Z*)-$CH_3(CH_2)_3CH$=$CHBr$	3.00	2/1	100	10	$CH_3(CH_2)_3CH$=$CHCH$=$CHCONH_2$ (*E,E*, 65; *E,Z*, ~20[g])
(*E*)-CH_3CH=$CHCO_2H$	(*E*)-$BrCH$=$C(CH_3)CO_2H$[h]	6.00	2/4	100	10	(*E,E*)-$HO_2CC(CH_3)$=$CHC(CH_3)$=$CHCO_2H$ (75)
	(*E*)-$BrCH$=$C(CH_3)CO_2CH_3$[h]	6.00	2/1	100	13	(*E,E*)-HO_2CCH=$C(CH_3)CH$=$C(CH_3)CO_2CH_3$ (82)
(*E*)-CH_3CH=$CHCO_2CH_3$	(*E*)-$HO_2CC(CH_3)$=$CHBr$	6.00	4/2	100	10	(*E,E*)-$HO_2CC(CH_3)$=$CHC(CH_3)$=$CHCO_2CH_3$ (76)
	(*E*)-$CH_3O_2CC(CH_3)$=$CHBr$	3.00	2/1	100	24	(*E,E*)-$CH_3O_2CC(CH_3)$=$CHC(CH_3)$=$CHCO_2CH_3$ (83)
CH_2=$C(CH_3)CO_2CH_3$	$(CH_3)_2C$=$CHBr$	3.00	6/2	100	28	$(CH_3)_2C$=$CHCH$=$C(CH_3)CO_2CH_3$ (*E*, 62; *Z*, 16)
	(*Z*)-$CH_3(CH_2)_3CH$=$CHBr$	1.25	2/1	100	15 days	$CH_3(CH_2)_3CH$=$CHCH$=$C(CH_3)CO_2CH_3$ (*E,E*, 49; *E,Z*, 14; *Z,E*, 5)

			PPh$_3$/Pd(OAc)$_2$ = 2/1			
		2.50		100	15 days	$CH_3(CH_2)_3CH{=}CHCH{=}C(CH_3)CO_2CH_3$ (*E,E*, 64; *E,Z*, 30; *Z,E*, 6)
			PPh$_3$/Pd(OAc)$_2$ = 6/3			
		2.50		100	5 days	$CH_3(CH_2)_3CH{=}CHCH{=}C(CH_3)CO_2CH_3$ (*E,E*, 20; *E,Z*, 40; *Z,E*, 3)
$CH_2{=}C(CH_3)CO_2CH_3$	(*E*)-$CH_3(CH_2)_3CH{=}CHI$	3.00	6/2	125	72	$CH_3(CH_2)_3CH{=}CHCH{=}C(CH_3)CO_2CH_3$ (*E,E*, 45; *E,Z*, 13; *Z,E*, 5)
	(*Z*)-$C_2H_5CH{=}C(I)C_2H_5$	3.00	2/1	125	16	$C_2H_5CH{=}C(C_2H_5)CH{=}C(CH_3)CO_2CH_3$ (*E,Z*, 49; *E,Z*, 31), unknown isomer (8)
	1-bromocyclohexene	3.00	2/1	100	64	(*E*)-(1-C_6H_9)$CH{=}C(CH_3)CO_2CH_3$ (44), (1-C_6H_9)$CH_2C(=CH_2)CO_2CH_3$ (35)
$CH_2{=}C(CH_3)CONH_2$[f]	$(CH_3)_2C{=}CHBr$	3.00	2/1	100	72	(*E*)-$(CH_3)_2C{=}CHCH{=}C(CH_3)CONH_2$ (71)
(*E*)-$CH_3O_2CCH{=}CHCO_2CH_3$	$(CH_3)_2C{=}CHBr$	3.00	4/2	100	44	(*E,E*)-$CH_3(CH_2)_2CH{=}C(CO_2CH_3)CH_2CO_2CH_3$ (59)
	(*Z*)-$CH_3(CH_2)_3CH{=}CHBr$	3.00	2/1	100	24	(*E,E*)-$CH_3(CH_2)_2CH{=}CHCH{=}C(CO_2CH_3)CH_2CO_2^-CH_3$ (80)
$CH_2{=}C(CO_2CH_3)CH_2CO_2CH_3$	$CH_3C(Br){=}CH_2$	3.00	2/1	100	48	(*E*)-$CH_2{=}C(CH_3)CH{=}C(CO_2CH_3)CH_2CO_2CH_3$ (50)

[a] The molar ratio of unsaturated acid derivative to vinylic halide was 1.25 except where noted. [b] Based upon mole percent of catalyst component employed compared to the vinylic halide. [c] Diels–Alder reaction products of the dienoic acid derivative and methyl acrylate. [d] THP = tetrahydropyranyl group. [e] Yield based upon the acrylonitrile present. [f] 4 mL of acetonitrile added as solvent to dissolve the amide. [g] A viscous liquid residue contained the *E,Z* isomer, but it was not purified. [h] Unsaturated acid to vinyl halide ratio = 1:1. [i] Isomer yields in mixtures determined by GLC.

Scheme I



R and R′ = alkyl groups; Q = CO_2^-, CO_2R, CN, $CONH_2$; X = Br or I

the related acrylic ester or amide and these, in turn, are a little more reactive than crotonic acid or its methyl ester.

Vinylic iodides are generally more reactive than bromides.[1] The difference may be relatively large. In the reaction of the (*Z*)-3-halo-3-hexenes with acrylonitrile, the iodo compound is at least 20 times more reactive than the bromo compound. Similarly, 2-iodo-1-hexene is about 35 times more reactive than the related bromide in the reaction with methyl acrylate at 100 °C.

The reaction rates appear to be directly proportional to the amount of palladium acetate used. We have normally employed 1 mol % palladium acetate based upon the vinylic halide as catalyst, but in reactions of polysubstituted reactants the rates may be very slow with this concentration of catalyst. In several examples we have used 3 mol % to shorten the reaction times. It is advantageous to increase reaction rates in cases where the starting materials and/or products isomerize thermally under the reaction conditions and in cases where the Diels–Alder reaction competes with the vinylic halide–olefin reaction.

The Diels–Alder reaction consumed essentially all of the dienoate ester produced (by reaction with methyl acrylate) in the reaction of 2-bromo-1-hexene with methyl acrylate, even with 3 mol % catalyst. The Diels–Alder reaction became insignificant, however, when the more reactive 2-iodo-1-hexene was used in place of the bromide.

Mechanism and Stereochemistry. The vinylic halide–acrylic acid derivative reactions can be explained on the basis of the mechanism proposed previously[1,2] (see Scheme I). The active catalyst is formed by reduction of the palladium(II) acetate added. In the presence of a phosphine it is presumably the bis(triarylphosphine)palladium(0) complex that is formed while reactants, solvent, amine, or halide ion will be the ligands in the absence of a phosphine. This species then oxidatively adds the vinylic halide with retention of the vinylic structure and the adduct adds to the olefinic double bond. With olefins sub-

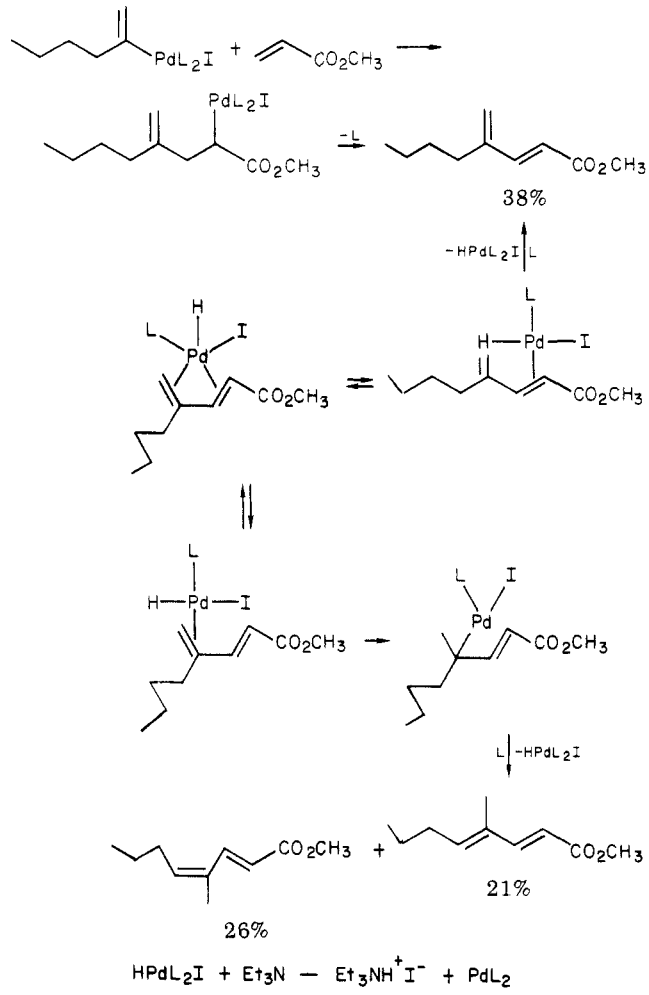
(2) R. F. Heck and B. Patel, "Catalysis in Organic Synthesis", Academic Press, Inc., New York, 1980, p 195.

stituted with strongly electron-withdrawing groups, such as the carboxyl, carbomethoxy, nitrile, or amide groups in the present examples, the direction of addition is totally specific. The vinylic group adds to the carbon farther from the electron-withdrawing group. This addition occurs in a completely syn manner. The adduct next undergoes an internal elimination of a hydridopalladium halide group, which forms a π complex with the conjugated diene produced. The elimination also is a selective syn reaction. If the hydridopalladium halide group is now displaced from the π complex, the diene formed possesses the stereochemistry of the vinylic halide in one double bond and the inverted stereochemistry of the reactant olefin in the other double bond. Alternatively, the hydridopalladium halide π complex may form an allylic, σ derivative which will go on to a π-allylic palladium complex with the allylic double bond. The π-allylic complex, unfortunately, rapidly equilibrates isomers through rotating σ forms. This causes loss of stereochemistry and the product ultimately formed by the hydridopalladium halide elimination and dissociation process will be the isomer formed from the (most stable) π-allylic complex, the isomer with the largest 1 and 3 substituents in the syn position relative to the central allylic carbon substituent.

Fortunately, the stereospecific reaction course can be favored (in the few cases where it is necessary) simply by increasing the concentration of the triarylphosphine in the reaction mixture. Triphenylphosphine is usually more effective for this purpose than tri-*o*-tolylphosphine. We believe the ligand concentration influences the fate of the product diene π complex with the hydridopalladium halide. The second-order displacement of the hydrido group by the phosphine becomes more important than the hydride readdition as the phosphine concentration is increased. This, of course, favors the stereospecific reaction path. This effect was noted previously in the reaction of the 1-bromo-1-hexene isomers with methyl acrylate.[1] The iodo derivative is less selective in its reactions than the bromide. The maximum selectivity we achieved previously from the most easily isomerized reactants, the (*Z*)-1-bromo-1-hexene and methyl acrylate, was 79% (*E,Z*)-methyl nonadienoate and 13% of the *E,E* isomer. We have repeated this reaction under different conditions. The reaction with 2:1 triphenylphosphine/palladium acetate as catalyst at 125 °C required 96 h to reach completion and produced 51% *E,Z* ester, 35% *E,E*, and ~3% of the presumed *Z,Z* isomer. Since we have now observed that both the 1-bromo-1-hexene reactant and the (*E,Z*)-methyl nonadienoate product undergo a slow thermal isomerization under the reaction conditions, we have increased the palladium catalyst concentration to minimize such isomerizations. This change, coupled with an increase in the triphenylphosphine concentration by a factor of three, produced 76% of the *E,Z* ester, only 4% of the *E,E* compound, and still about 4 or 5% of the presumed *Z,Z* isomer. The *Z,Z* isomer must be arising from elimination of the other available hydrogen with the hydridopalladium halide group to form the cis α,β double bond.

An alternative explanation for the isomerization of the γ,δ double bond of the dienoate esters seems more attractive in another example and could apply to the above example as well. The 2-iodo-1-hexene reaction with methyl acrylate, using a 6:3 catalyst to minimize the Diels-Alder reaction, produced a mixture of dienoate ester products: 38% of the expected, (*E*)-methyl 4-*n*-butyl-2,4-pentadienoate, 26% (*E,E*)-methyl 4-methyl-2,4-octadienoate, and 21% of the *E,Z* isomer of the last compound. The mechanism involving the π-allylic intermediate given above

Scheme II

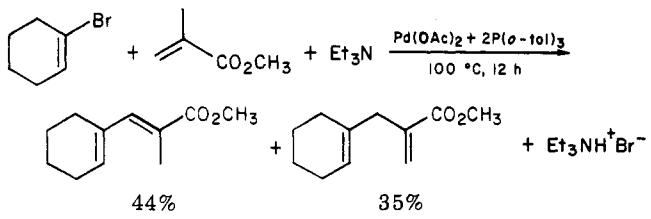


is not adequate to explain the formation of the last two products, since simple elimination from the π-allylic intermediate cannot produce these isomers. A reasonable explanation of this isomerization is that the hydridopalladium iodide group in the π complex with the diene is transferred intramolecularly from the α,β double bond to the γ,δ double bond via a bidentate diene complex (Scheme II). Unfortunately, we were unable to improve the selectivity of this reaction by treating the bromide with a 3:6 catalyst because even under these conditions Diels–Alder adducts were the major products.

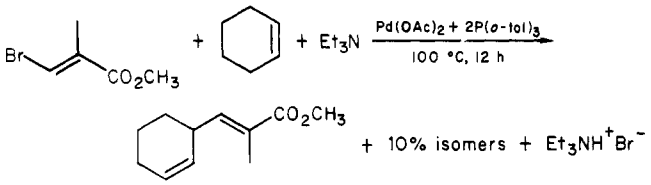
It is quite possible that π-allylic complexes are formed in this reaction also, but they are not required to explain the products formed. Whether or not the hydridopalladium halide group shifts from one double bond to another in other cases is not clear. Most probably, both π-allylic complexes and the hydrido shift mechanism can occur in all of the examples.

The reaction of 1-bromocyclohexene with methyl methacrylate is the only example in which a significant amount of elimination to a nonconjugated diene occurred. In this reaction, the major product (44%) was the expected (*E*)-methyl 3-(1′-cyclohexenyl)-2-methylacrylate, while 35% of the product was methyl 2-(1′-cyclohexenyl-1′-methyl)acrylate. Presumably, the conformation of the organopalladium intermediate is not as favorable for elimination to the conjugated diene in this case as it is in the open-chain cases studied.

The reverse combination of (*E*)-methyl 3-bromo-2-methylacrylate and cyclohexene gives mainly another isomeric product, (*E*)-methyl 3-(3-cyclohexenyl)-2-

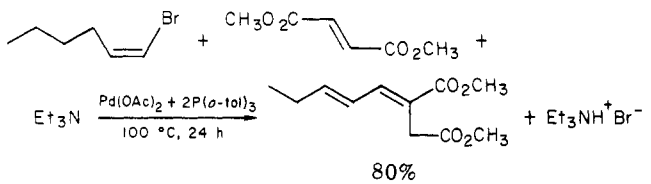


methylacrylate in 57% yield, as might be expected by the usual mechanism, since a syn elimination of the hydridopalladium group from the intermediate to form the conjugated diene is not possible.

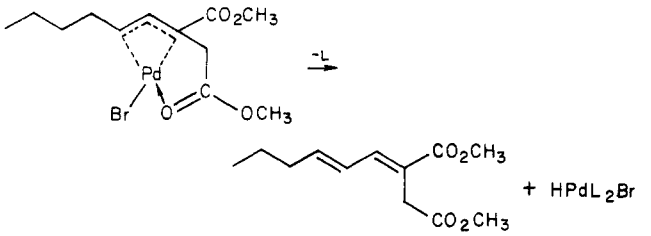


We also examined the reaction of this bromo ester with 2-methyl-1-pentene, since we anticipated that the reverse halide–olefin combination would react very slowly. This reaction produced 50% (*E,E*)-methyl 2,5-dimethyl-1,3-octadienoate and 16% of the *E,Z* isomer.

The reactions of vinylic bromides with dimethyl fumarate require some discussion, since the products formed are not the ones that might have been expected by either of the mechanisms proposed above. 1-Bromo-2-methyl-1-propene yields 59% (*E*)-methyl 3-(carbomethoxy)-5-methyl-3,5-hexadienoate as the only isolable product while in the same reaction (*Z*)-1-bromo-1-hexene gave 80% (*E,E*)-methyl 3-(carbomethoxy)-3,5-nonadienoate.

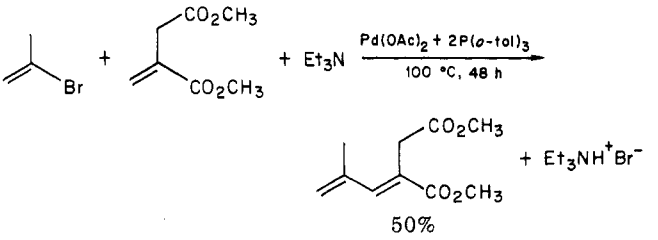


In both examples a simple elimination of the hydridopalladium bromide group would have given 2,4-dienoate esters rather than the observed 3,5 isomers. A possible explanation is that both reactions proceed by way of 3,4,5-π-allylic palladium complexes and that the terminal carbomethoxyl group is coordinated to the palladium in the π complex. The elimination, then, probably would only be favorable for the formation of the 3,5 isomer.



It is interesting that 2-bromopropene reacts with dimethyl itaconate to form the same product obtained from 1-bromo-2-methyl-2-propene and dimethyl fumarate, in 50% yield.

Synthetic Utility. The examples in Table I clearly show that particularly methyl acrylate reacts selectively with a variety of vinylic halides to give stereospecific reaction products in good yields. Therefore, these reactions are preparatively useful. Limited work with the free acid and acrylamide suggest they are very similar to the ester.



Acrylonitrile reacts also, but more cis α,β double bond is produced than with the other acrylic acid derivatives. Crotonic acid and its methyl ester react well with the very reactive 3-bromo-2-methylacrylic acid or its ester, but less reactive halides generally give low yields of dienoic acid derivatives in very slow reactions. Methyl methacrylate reacts fairly readily with all types of vinylic halides, but mixtures of isomers are generally formed. Increasing the phosphine concentration and the palladium concentration are helpful in the 1-bromo-1-hexene reaction, but because the reaction rate is lower than with the related methyl acrylate reaction a high yield of a single isomer could not be obtained. Significant amounts of dienoates with *Z* stereochemistry at the α,β double bond, are formed in the methyl methacrylate reactions and we are unable to control the formation of these isomers. Possibly, these isomers could be isomerized to the (*E,E*)-2,4-dienoates, but we have not investigated the isomerization. Methacrylamide is perhaps a better reactant to use for introducing the methacryl unit, since the amides are generally solids and usually may be purified by recrystallization. 1-Bromo-2-methyl-1-propene and methacrylamide gave a 71% yield of (*E*)-2,5-dimethyl-2,4-hexadienoic acid amide after recrystallization to remove other isomers which presumably were present. Finally, dimethyl fumarate gave essentially one isomeric product with, at least, two vinylic halides and the reaction is preparatively useful.

It should be pointed out that the reactions described here are particularly useful for preparing highly functionalized products. Note, for example, the several reactions which gave conjugated dienedioic acid derivatives, one which formed a conjugated dienoate acetal, and another which gave a pyranyl ether of a hydroxy dienoate. (The free aldehyde and the free hydroxyl reactants did not give identifiable products in the reaction.)

Experimental Section

The physical properties, NMR spectra, and molecular weights as determined by high-resolution mass spectroscopy of the new compounds prepared in this study are given in Table II (Supplementary Material).

Reagents. The olefinic reactants were all commercially available samples. (*E*)-2-Bromo-2-butene (Columbia Org. Chem. Co.) and 2-bromopropene (Chem. Samples Co.) were used as received from commercial sources. 2-Bromo-2-methyl-2-butene,[3] (*Z*)-1-bromo-1-hexene,[3] 1-bromo-2-methyl-1-propene,[4] 3-bromo-2-methylpropenal dimethyl acetal,[3] (*E*)-methyl 3-bromo-2-methacrylate,[5] (*E*)-3-bromo-2-methacrylic acid,[6] and 1-bromo-1-cyclohexene[7] were prepared by literature methods. The 3-bromoallyl alcohol tetrahydropyranyl ether was prepared from the alcohol[8] and dihydropyran with acetic acid as catalyst (90% yield, bp 100–110 °C (10 mm)). (*Z*)-3-Bromo-3-hexene, bp 34 °C (16 mm), and (*Z*)-3-iodo-3-hexene, bp 43–44 °C (10 mm), were obtained by heating 3-hexyne with the concentrated aqueous acids

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(5) H. A. Dieck and R. F. Heck, *J. Am. Chem. Soc.*, **96**, 1133 (1974).
(6) C. Kolbe, *J. Pract. Chem.*, **25**, 382 (1882).
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(8) L. F. Hatch and K. E. Harwell, *J. Am. Chem. Soc.*, **75**, 6002 (1953).

until substantially all the acetylene had reacted. Other halides were prepared as described below.

The palladium acetate, phosphines, and amines used were the same as those employed in our previous work.[1,3]

2-Bromo-1-hexene. Iron filings (1 g) were dissolved in 120 mL of 48% aqueous hydrobromic acid. To this was added 41 g (0.5 mol) of 1-hexyne (Chem. Samples Co.) and the two-phase mixture was stirred under a reflux condenser at 50 °C for 2 days. The organic layer was then separated, washed with water, dried with magnesium sulfate, and distilled. There was obtained a 50% yield of 2-bromo-1-hexene, bp 133–134 °C. 2-Hexanone, 20%, was obtained as a byproduct.

2-Iodo-1-hexene. A mixture of 41 g (0.5 mol) of 1-hexyne and 136 mL of 47% aqueous hydriodic acid was stirred at room temperature for 5 days. The organic layer was separated, washed with aqueous sodium thiosulfate and then with water, and dried. Distillation gave a 73% yield of 2-iodo-1-hexene, bp 88–92 °C (82 mm).

(*E*)- and (*Z*)-1-Bromo-2-methyl-1-pentenes. 2-Methyl-1-pentene (67 g, 0.8 mol) in 300 mL of chloroform was cooled to 0 °C and 120 g (0.8 mol) of bromine dissolved in 300 mL of chloroform was added slowly with stirring, while keeping the temperature of the reaction mixture below 5 °C. After the addition, the solution was distilled. The dibromide, bp 82–83 °C (15 mm), was obtained in 60% yield.

Dehydrobromination was achieved by adding 122 g (0.5 mol) of the dibromide slowly to a solution of 80 g (1.42 mol) of potassium hydroxide dissolved in 196 g of ethylene glycol while this solution was stirred and heated at ca. 150 °C. The product was allowed to distill from the reaction mixture as it was formed. The organic phase of the distillate was separated, dried, and fractionated through a spinning-band column. The *Z* isomer distilled first, bp 29–30 °C (50 mm), followed by the *E* isomer, bp 30–31.5 °C (50 mm). The ratio of *E*:*Z* was about 10:1 and the total yield was 80% based upon the dibromide.

General Procedure for the Preparation of 2,4-Dienoic Acid Derivatives. Mixtures of 10 mmol of the vinylic halide, 12.5 mmol of the olefinic compound, 30 mmol of triethylamine, 0.10 mmol of palladium acetate, and 0.20 mmol of triphenyl- or tri-*o*-tolylphosphine were shaken until homogeneous in capped tubes or bottles and then placed in either a steam bath or oil bath at the appropriate temperature. Small samples were removed from the reaction mixture periodically and analyzed by GLC. Listed in Table I are the times at which the vinylic halide had disappeared or no longer decreased. Products were isolated by rinsing the cooled reaction mixtures with ether into excess 10% aqueous sodium hydroxide. The mixtures were shaken and separated, and the organic phases were dried and concentrated in a rotary evaporator. Products were separated from the crude mixtures by GLC, distillation, or recrystallization. Generally reactions were scaled up by a factor of five or ten for isolation of products. In reactions where free carboxylic acids were reactants, products were isolated by treatment of the reaction mixtures with 4% aqueous hydrochloric acid rather than with base. In the reaction of 3-bromo-2-methacrylic acid with crotonic acid and of methyl 3-bromo-2-methylacrylate with crotonic acid, the reactants were present in equal concentrations in order to facilitate purification of the reaction products by crystallization. Acetonitrile (8 mL/10 mmol of halide) was used as solvent in the reactions of acrylamide and methacrylamide because of their low solubilities.

When yields of products were determined by GLC, inert internal standards were added to the initial reaction mixtures and yields were calculated by using predetermined response factors for each product.

Some specific examples of the reaction are given below.

(*E*)-4,5-Dimethyl-2,4-hexadienoic Acid. A mixture of 1.49 g (10 mmol) of 2-bromo-3-methyl-2-butene, 0.90 g (12.5 mmol) of acrylic acid, 3.04 g (30 mmol) of triethylamine, 0.022 g (0.10 mmol) of palladium acetate, and 0.061 g (0.20 mmol) of tri-*o*-tolylphosphine was placed in a 20-mL heavy-walled Pyrex tube and the tube was capped. After the catalyst was dissolved by shaking, the solution was heated in an oil bath at 125 °C for 43 h. At this time the starting bromide had disappeared as determined by GLC. After cooling at room temperature the reaction mixture was stirred with 4% aqueous hydrochloric acid and the product was extracted with several portions of ether. After being dried the extracts were concentrated in a rotary evaporator and the solid acid obtained was recrystallized from hexane. The colorless crystals of acid were obtained in 85% yield, mp 155–156 °C.

(*E*,*E*)-Methyl 3-Ethyl-2,4-heptadienoate. A mixture of 10.5 g (50 mmol) (*Z*)-3-iodo-3-hexene, 6.32 g (62.5 mmol) of methyl methacrylate, 15.17 g (150 mmol) of triethylamine, 0.11 g (0.50 mmol) of palladium acetate, and 0.305 g (1.00 mmol) of tri-*o*-tolylphosphine in a capped Pyrex bottle was heated at 125 °C in an oil bath for 24 h. GLC showed the iodide had all reacted at this time. The reaction mixture was cooled and diluted with ether and 10% aqueous sodium hydroxide. After the phases were separated, the ether layer was dried and distilled to give an 86% yield of the ester product, bp 69–70 °C (1 mm).

(*E*,*E*)-5-(Carbomethoxy)-3,5-dimethyl-2,4-hexadienoic Acid. A mixture of 7.16 g (40 mmol) of (*E*)-methyl 3-bromo-2-methylacrylate, 3.49 g (40 mmol) of (*E*)-crotonic acid, 24.2 g (240 mmol) of triethylamine, 0.088 g (0.40 mmol) of palladium acetate and 0.244 g (0.80 mmol) of tri-*o*-tolylphosphine was heated in a capped Pyrex bottle in a steam bath for 15 h. At this time GLC analysis showed the absence of starting bromide. Isolation of the product as in the (*E*)-4,5-dimethyl-2,4-hexadienoic acid preparation above gave an 82% yield of the acid ester after crystallization from hexane, mp 111–112 °C.

(*E*)-2,5-Dimethyl-2,4-hexadienoic Acid Amide. A mixture of 6.75 g (50 mmol) of 1-bromo-2-methyl-1-propene, 5.32 g (62.5 mmol) of methacrylamide, 15.18 g (150 mmol) of triethylamine, 0.11 g (0.50 mmol) of palladium acetate, 0.305 g (1.00 mmol) of tri-*o*-tolylphosphine, and 40 mL of acetonitrile as solvent in a capped Pyrex bottle was heated in a steam bath for 72 h. Isolation of the product by ether extraction from the base-treated crude reaction mixture as in the (*E*,*E*)-methyl 3-ethyl-2,4-heptadienoate example above gave a solid after removal of the ether solvent. Recrystallization from aqueous methanol gave a 71% yield of the amide, mp 141–142 °C.

Acknowledgment. We thank the National Science Foundation for a grant which supported this investigation. The palladium acetate used was kindly loaned to us by the Johnson Matthey Co., Inc.

Registry No. (*E*)-4,5-Dimethyl-2,4-hexadienoic acid, 76232-19-4; methyl (*E*,*E*)-4-methyl-2,4-hexadienoate, 57258-50-1; methyl (*E*,*Z*)-4-methyl-2,4-hexadienoate, 76232-20-7; dimethyl (*E*,*E*)-2,4-dimethyl-2,4-hexadienedioate, 76232-21-8; methyl (*E*,*Z*)-2,4-nonadienoate, 39924-44-2; methyl (*E*,*E*)-2,4-nonadienoate, 54354-51-7; methyl (*E*,*E*)-5-methyl-2,4-octadienoate, 76232-22-9; methyl (*E*,*Z*)-5-methyl-2,4-octadienoate, 76232-23-0; (*E*)-1-bromo-2-methyl-1-pentene, 76232-24-1; (*Z*)-1-bromo-2-methyl-1-pentene, 66124-74-1; 2-bromo-1-hexene, 3017-66-1; 2-iodo-1-hexene, 54145-19-6; methyl (*E*)-4-butyl-2,4-pentadienoate, 76232-25-2; methyl (*E*,*E*)-4-methyl-2,4-octadienoate, 76232-26-3; methyl (*E*,*Z*)-4-methyl-2,4-octadienoate, 76232-27-4; methyl (*E*,*Z*)-4-ethyl-2,4-heptadienoate, 76232-28-5; methyl (*E*,*E*)-4-ethyl-2,4-heptadienoate, 76232-29-6; methyl (*E*,*E*)-5-methyl-6,6-dimethoxy-2,4-hexadienoate, 76232-30-9; methyl (*E*,*E*)-6-(tetrahydropyranyloxy)-2,4-hexadienoate, 76232-31-0; methyl (*E*)-3-(1-cyclohexenyl)-2-propenoate, 54526-84-0; (*E*,*Z*)-4-ethyl-2,4-heptadienenitrile, 76232-32-1; (*Z*,*Z*)-4-ethyl-2,4-heptadienenitrile, 76232-33-2; 3-(diethylamino)propanenitrile, 5351-04-2; (*E*,*E*)-2,4-nonadienamide, 76232-34-3; (*E*,*E*)-2,4-hexadienedioate, 76232-35-4; methyl (*E*,*E*)-2,4-dimethyl-5-carboxy-2,4-pentadienoate, 76232-36-5; methyl (*E*,*E*)-3,5-dimethyl-5-carboxy-2,4-pentadienoate, 76232-37-6; methyl (*E*)-2,5-dimethyl-2,4-hexadienoate, 76232-38-7; methyl (*Z*)-2,5-dimethyl-2,4-hexadienoate, 76232-39-8; methyl (*E*,*E*)-2-methyl-2,4-nonadienoate, 61382-50-1; methyl (*E*,*Z*)-2-methyl-2,4-nonadienoate, 75066-90-9; methyl (*Z*,*E*)-2-methyl-2,4-nonadienoate, 76232-40-1; methyl (*E*,*Z*)-4-ethyl-2-methyl-2,4-heptadienoate, 76232-41-2; methyl (*Z*,*Z*)-4-ethyl-2-metyl-2,4-heptadienoate, 76232-42-3; methyl (*E*)-3-(1-cyclohexenyl)-2-methyl-2-propenoate, 76232-43-4; methyl 2-(cyclohexenylmethyl)-2-propenoate, 76232-44-5; methyl (*E*)-2-(cyclohexen-3-yl)-2-butenoate, 76232-45-6; methyl (*E*,*E*)-2,4-dimethyl-2,4-octadienoate, 76232-46-7; methyl (*E*,*Z*)-2,4-dimethyl-2,4-octadienoate, 76232-47-8; 2-propenoic acid, 79-10-7; methyl 2-propenoate, 96-33-3; 2-propenenitrile, 107-13-1; 2-propenamide, 79-06-1; (*E*)-2-butenoic acid, 107-93-7; methyl 2-butenoate, 623-43-8; methyl 2-methyl-2-propenoate, 80-62-6; 2-methyl-2-propenamide, 79-39-0; dimethyl (*E*)-butenedioate, 624-49-7; dimethyl methylenebutanedioate, 617-52-7; 2-bromo-3-methyl-2-butene, 51872-48-1; (*E*)-2-

bromo-2-butene, 3017-71-8; methyl (*E*)-3-bromo-2-methyl-2-propenoate, 40053-01-8; (*Z*)-1-bromo-1-hexene, 13154-12-6; (*E*)-3-iodo-3-hexene, 16403-09-1; (*E*)-3-bromo-2-methyl-1,1-dimethoxy-2-propene, 76232-48-9; 1-bromocyclohexene, 2044-08-8; 1-bromo-3-(tetrahydropyranyloxy)-1-propene, 76232-49-0; (*Z*)-3-iodo-3-hexene, 16403-13-7; (*Z*)-3-bromo-3-hexene, 16645-01-5; (*Z*)-1-bromo-1-hexene, 13154-12-6; (*E*)-3-bromo-2-methyl-2-propenoic acid, 24557-13-9; methyl (*E*)-3-bromo-2-methyl-2-propenoic acid, 40053-01-8; 1-bromo-2-methyl-1-propene, 3017-69-4; 1-iodo-1-hexene, 16644-98-7; (*Z*)-3-iodo-3-hexene, 16403-13-7; 2-bromo-1-propene, 557-93-7; (*Z*)-4,5-dimethyl-2,4-hexadienoic acid, 76232-50-3; dimethyl (*E,E*)-2-methyl-2,4-hexadienedioate, 39995-94-3; (*E,Z*)-2,4-nonadienamide, 76232-51-4; (*E*)-2,5-dimethyl-2,4-hexadienamide, 76232-52-5; dimethyl 2-(2-methylenepropylidenyl)butanedioic acid, 76232-53-6; dimethyl 2-(2-hexenylidenyl)butanedioic acid, 76232-54-7; $Pd(OAc)_2$, 3375-31-3.

Supplementary Material Available: Table II listing the physical properties, NMR spectral data, and molecular weights (high-resolution mass spectroscopy) for the new compounds prepared (7 pages). Ordering information is given on any current masthead page.

Thermal Rearrangement of a 2-Methylenebicyclo[2.1.1]hexane

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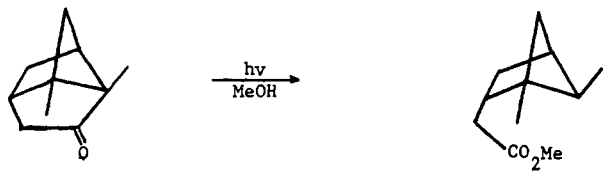
Received July 7, 1980

Pyrolysis of 1,*exo*-5-dimethyl-2-[(carbomethoxy)methylene]bicyclo[2.1.1]hexane results in isomerization of the 5-methyl group to the endo configuration. A homolytic cleavage mechanism of the vinylcyclobutane system is proposed to explain this unexpected result.

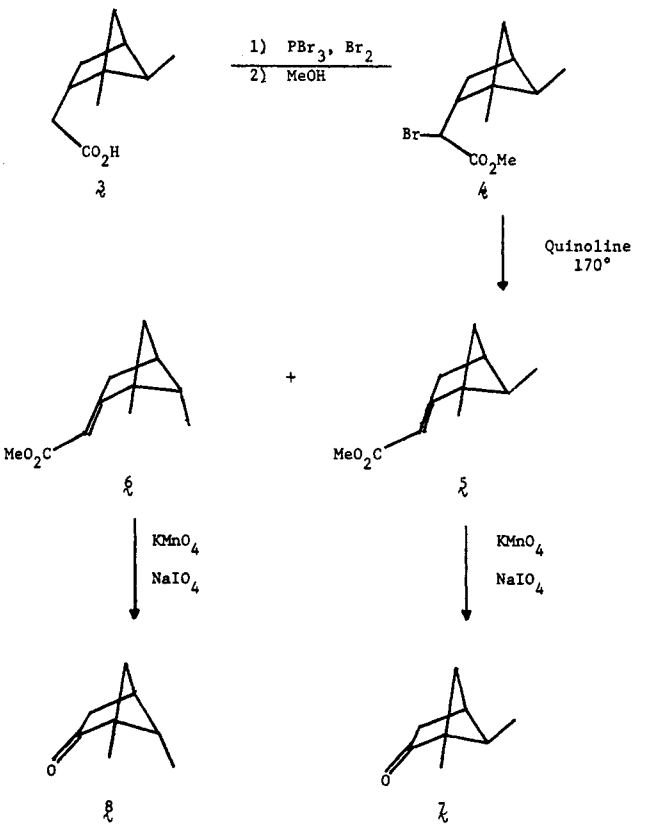
During work on the photochemical behavior of carvone camphor[1] **1**, we devoted extensive effort to development of a degradation method to prove unambiguously the structure and stereochemistry of the photolysis product **2**. This work ultimately showed that **2** is the exclusive



1 **2**

product of the photolytic process, in accord with results obtained by others.[2] In one degradation attempt (Scheme I) bromination of the acid **3** with Br_2/PBr_3 followed by methanolysis gave a 1:1 mixture of bromo esters **4**. Dehydrobromination of **4** by quinoline at 170 °C resulted in the formation, in variable amounts, of two unsaturated esters which could not be isolated in good purity because of their instability during preparative gas chromatography. Data obtained on impure samples strongly suggested the structures **5** and **6** in which one product apparently resulted from rearrangement during one of the steps of the degradation sequence. Confirmation of the structure of the ring portion of ester **5** was obtained by oxidation of a partially purified sample to the known ketone **7**, which was identical with the sole product obtained by an alternate degradation sequence of **3**.[1] Oxidation of **6** gave a different ketone, establishing that **5** and **6** did not differ simply in the configuration of the double bond. The ketone showed properties in excellent agreement with those predicted for **8** [e.g., ν 1754 cm^{-1}; δ 0.79 (3 H, d, 5-endo CH_3)], but an unambiguous structure proof was lacking. In subsequent work, presented in this paper, we have confirmed the structure of ketone **8** by an unambiguous synthesis, established the complete structures of esters **5**

Scheme I



3 **4** **6** **5** **8** **7**

and **6**, and determined that the ester **6** is the result of a thermal rearrangement of **5**.

Synthesis of 8. The method developed for preparation of **8** is shown in Scheme II. The original intent was to generate the bicyclic ketones by photocyclization of the ketone corresponding to alcohol **9**,[3] but all attempts to oxidize **9** failed. This problem was overcome by using a

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