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(12) The diol **8** is secreted together with a pyrrolizidinone (ketone) by brushlike hair pencil glands on the abdomen of males of the queen butterfly (*Donus gilippus berenice*). During mating, the male uses these glands to deposite a dustlike pheromone on the antennae of the female; the ketone appears to act as an aphrodesiac, while the function of the diol appears to be simply that of a glue, securing the attachment of the pheromonal dust to the female antennae. For a description of the biology, see (a) T. E. Pliske and T. Eisner, *Science*, **164**, 1170 (1969), and (b) D. Schneider and U. Seibt, *ibid.*, **164**, 1173 (1969). For chemical studies, see (c) J. Meinwald, Y. C. Meinwald, and P. H. Mazzocchi, *ibid.*, **164**, 1174 (1969), and (d) D. H. Miles, P. Loew, W. S. Johnson, A. F. Kluge, and J. Meinwald, *Tetrahedeon Lett.*, 3019 (1972).

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(14) E. J. Corey, K. Achiwa, and J. A. Katzenellenbogen, *J. Amer. Chem. Soc.*, **91**, 4318 (1969).

(15) Attempts to prepare this alcohol directly by the rearrangement of 6,7-oxidogeranyl mesitoate using lithium diisopropylamide or lithium di-*n*-butylamide [see C. L. Kissel and B. Rickborn, *J. Org. Chem.*, **37**, 737 (1972)] were uniformly unsuccessful.

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Palladium-Catalyzed Carboalkoxylation of Aryl, Benzyl, and Vinylic Halides

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Received June 18, 1974

Aryl and vinylic bromides and iodides and benzyl chloride react with carbon monoxide and an alcohol at 100° or below and atmospheric pressure in the presence of a tertiary amine and a catalytic amount of a palladium–triphenylphosphine complex to form esters. The reaction is tolerant of a variety of functional groups and shows appreciable stereospecificity at 60–80° with cis and trans vinylic halides producing esters with retained configuration.

In previous papers we and others have noted the ready formation of organopalladium complexes by reaction of finely divided palladium metal[1,2] or palladium(0)–organophosphine complexes[3,4] with aryl, benzyl, and vinyl halides.

Since these organopalladium complexes reacted easily with olefins,[1-3] it seemed reasonable to expect that they would also react with carbon monoxide to form acylpalladium derivatives. The last compounds could then possibly reductively eliminate acyl halide or at least react with alcohols to form esters and an unstable metal hydride which could re-form the palladium(0) starting material. Therefore a catalytic synthesis of acyl halides or esters from aryl, benzyl, and vinyl halides and carbon monoxide appeared possible analogous to the known reactions of allylic chlorides.[5,6] A similar reaction is known to occur with bromo-π-allylnickel(II) dimer, from allyl bromide and tetracarbonylnickel(0), and carbon monoxide.[7] A related carboalkoxylation of organomercury compounds with palladium salts, carbon monoxide, and an alcohol is known, but generally mixtures of esters, biaryls, and ketones were obtained with only low yields of esters being formed in most instances.[8,9] Tetracarbonylnickel(0) is an excellent reagent for the carboalkoxylation of aryl, benzyl, and vinyl halides particularly in the presence of bases.[10,11] The nickel reaction has two problems which we hoped to overcome by the use of palladium catalysts: (1) tetracarbonylnickel vapor is extremely toxic while the palladium reagents are not volatile and (2) tetracarbonylnickel is either required in stoichiometric quantities or at least in relatively large catalytic amounts while the palladium complexes may react highly catalytically.

$$\begin{array}{l} \mathrm{H_2C{=}CHCH_2Cl + CO \xrightarrow{Pd} H_2C{=}CHCH_2COCl} \\ \qquad\qquad\qquad\quad \mathrm{\searrow\!\xrightarrow[ROH]{Pd} H_2C{=}CHCH_2COOR + HCl} \end{array}$$

Preliminary experiments showed that acyl halides were not formed catalytically from aryl halides at 100° and with 1 atm of carbon monoxide even in the presence of tertiary amines, but in the presence of an alcohol and a tertiary amine a highly catalytic reaction ensued forming esters in good yields.

$$\mathrm{ArX + CO + ROH + R_3'N \xrightarrow{"Pd"} ArCOOR + R_3'NH^+X^-}$$

Results

Initial experiments were carried out with aryl iodides adding palladium acetate as catalyst. The palladium(II) acetate was reduced by the carbon monoxide in the reaction mixture. Little carbon monoxide was absorbed at 100° and at 1 atm unless a tertiary amine and an alcohol were added. We used *n*-butyl alcohol as the alcohol and tri-*n*-butylamine as the tertiary amine, since they boiled well above the reaction temperature. Generally, the reactions with 1–2 mol % of catalyst at 100° required 14 hr or more to reach completion and were usually allowed to go longer to be sure the aryl halide had completely reacted. Reactions were carried out in a gasometric apparatus as described previously so that the reaction rate and the amount of gas absorbed could be measured.[12] Products were isolated by ether extraction, acid washing, and distillation. The esters were obtained very pure by this simple procedure. The yields and product properties of representative examples are show in Table I. Nmr data on the products are given in Table III which will appear in the microfilm edition of the journal. See paragraph at the end of paper regarding supplementary material. Substituent effects in the aromatic halide appeared to be less significant than in the reactions of the same halides with olefins.[1,3] Both strongly electron supplying and withdrawing substituents could be present.

The reaction with palladium acetate as catalyst at 100° was limited to aryl iodides; bromides did not react unless they were strongly activated with electron withdrawing substituents. We found, however, that adding 2 equiv of triphenylphosphine would cause unactivated aryl bromides to react at practical rates and produce esters in good yields. Aryl iodides reacted at about the same rates with the phosphine catalysts as they did with the palladium acetate cata-

Table I
Carbobutoxylation of Aryl and Benzyl Halides[a]

Halide	Catalyst	Reaction time, hr	$T_{1/2}$, min	Product (% yield)[b,c]	Bp, °C	Molecular weight Found	Molecular weight Calcd
C_6H_5I (591-50-4)	$Pd(OAc)_2$ (3375-31-3)	20	312	C_6H_5COO-*n*-Bu (70) (136-60-7)	100–110 (10 mm)[i]		
4-$CH_3OCOC_6H_4I$ (619-44-3)	$Pd(OAc)_2$	16		4-$CH_3OCOC_6H_4COO$-*n*-Bu (83) (52392-55-9)	133–134 (0.2 mm)	236.117	236.105
4-$CH_3OC_6H_4I$ (696-62-8)	$Pd(OAc)_2$	16		4-$CH_3OC_6H_4COO$-*n*-Bu (69) (6946-35-6)	114–115 (0.2 mm)[j]	208.107	208.110
2,6-$(CH_3)_2C_6H_3I$ (608-28-6)	$Pd(OAc)_2$	40		2,6-$(CH_3)_2C_6H_3COO$-*n*-Bu (63) (52392-56-0)	78–80 (0.4 mm)	206.122	206.130
C_6H_5I	$PhPdI(PPh_3)_2$ (18115-61-2)	30	467	C_6H_5COO-*n*-Bu (96)[d]		178.104	178.099
C_6H_5Br (108-86-1)	$PhPdBr(PPh_3)_2$ (33381-14-5)	24	718	C_6H_5COO-*n*-Bu (78)[d]			
C_6H_5Br (623-00-7)	$Pd_2Br_4(PPh_3)_2$[e] (M)	24	1376	C_6H_5COO-*n*-Bu			
4-NCC_6H_4Br[f]	$PdBr_2(PPh_3)_2$ (23523-33-3)	14		4-NCC_6H_4COO-*n*-Bu (89) (29240-34-4)	Mp 54–55[k]	203.095	203.095
1-$C_{10}H_7Br$ (90-11-9)	$PdBr_2(PPh_3)_2$	80	1367	1-$C_{10}H_7COO$-*n*-Bu (46)[g] (3007-95-2)	165–170 (19 mm)[l]	228.121	228.115
$C_6H_5CH_2Cl$ (100-44-7)	$PdCl_2(PPh_3)_2$ (13965-03-2)	40	1677	$C_6H_5CH_2COO$-*n*-Bu (45)[h] (122-43-0)	135–142 (22 mm)	192.122	192.115

[a] Reactions were carried out at 100° with 1 atm of CO, 17.2 mmol of halide, 0.25 mmol of catalyst, 21.2 mmol of *n*-butyl alcohol, and 19 mmol of tri-*n*-butylamine. Registry numbers are given in parentheses. [b] Yields are of isolated, pure products except where noted. [c] Products all showed strong ir bands at 1700–1750 cm^{-1} and all had nmr spectra consistent with the proposed structures. [d] Yields determined by glc with diphenyl ether as an internal standard. [e] Only 0.125 mmol of catalyst was used. [f] Reaction was carried out at 60° under 30 psi of CO in a capped bottle. [g] Reaction was only about 81% complete when the product was isolated. [h] Reaction was only about 65% complete when the product was isolated. [i] Reported bp 250°, "Handbook of Chemistry and Physics," 40th ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1959, p 846. [j] Reported bp 183° (40 mm), L. G. Radcliffe and W. A. Brindley, *Perfum. Essent. Oil Rec.*, 13, 414 (1922). [k] Reported mp 56–57°, F. E. D. Garigi and H. Gisvold, *J. Chem. Pharm. Ass.*, 38, 154 (1949). [l] Reported bp 151° (0.4 mm), G. B. Arrowsmith, G. H. Jeffery, and A. I. Vogel, *J. Chem. Soc.*, 2072 (1965).

lyst. Examples using the triarylphosphine procedure are also listed in Table I. In most instances purified dihalo- or haloarylbis(triphenylphosphine)palladium(II) complexes were used as catalysts although palladium(II) acetate with 2 equiv of triphenylphosphine produced identical catalysis as near as we could tell.

Table I contains two examples of particular interest. The carbobutoxylation of methyl *p*-iodobenzoate gave an 83% yield of *n*-butyl methyl terephthalate with none of the symmetrical esters being formed. The relatively hindered 2,6-dimethyliodobenzene also reacted normally at about half the rate of iodobenzene to form *n*-butyl 2,6-dimethylbenzoate in 63% yield.

The relative rates of reaction of the differently substituted aryl halides can be estimated from the half lives ($T_{1/2}$) listed in the table. The $T_{1/2}$ was the time required for half of the theoretical amount of CO to be absorbed. Electron withdrawing substituents increased and electron supplying groups decreased the reaction rates. The presence of the phosphine ligands appeared to slow the rate of the reaction of iodobenzene while it must have substantially increased the rate of reaction of bromobenzene since very little or no reaction occurred without the phosphine. With the phosphine catalyst iodobenzene was less than twice as reactive as bromobenzene. This is a remarkably small difference which suggests that oxidative addition may not be rate determining in this reaction. We attempted to measure relative rates of reaction by carrying out competitive reactions of pairs of aryl halides. We found as Cassar did with nickel carbonyl[11] that iodide ion was a very effective inhibitor for the reaction and when mixtures of aryl bromides and iodides were allowed to react the reactions proceeded at about the rates expected for the iodide but that the bromides did not react significantly. Calculating the relative rates of reaction of iodobenzene compared to bromobenzene in the presence of iodide ion (extrapolating back to zero time) from two pairs of relative rates measured where substituents were different gave the result that iodobenzene was 243 times more reactive than bromobenzene. This contrasts with the value of twice as reactive found by comparing half lives. Comparisons by the competitive method should be more meaningful for different aryl halides containing the same halogen. We found for example that 4-bromoanisole was 0.23 times and 4-bromobenzonitrile was 275 times as reactive as bromobenzene by this means. Cassar found the corresponding values for the same halide for his tetracarbonylnickel(0) catalyzed carboxylation were 0.4 and 108, respectively.[11] Apparently the palladium catalyst is more selective than nickel is. Both 1-bromoaphthalene and benzyl chloride were significantly less reactive than was bromobenzene in the carbobutoxylation reaction.

The triphenylphosphine–palladium complexes also catalyzed the carbobutoxylation of vinylic iodides and bromides in the presence of tertiary amines. The compounds studied and the yields of esters obtained from them are listed in Table II. The nmr spectra of the products are given in Table III which will appear in the microfilm edition of this journal. See paragraph at end of paper regarding supplementary material.

Cis- and trans vinylic halides were carbobutoxylated under various conditions to find optimum conditions for retaining the initial stereochemistry in the product. At 100° both *E*- and *Z*-3-iodo-3-hexene give mixtures of three carbobutoxy derivatives. Without triphenylphosphine, palladium acetate produces about equal amounts of the three products while with $PdI_2[P(C_6H_5)_3]_2$ as catalyst the major product was the one formed with retention of stereochemistry. The *E* iodide reacts at 100° about three times more

Table II
Carbobutoxylation of Vinylic Halides[a]

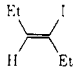
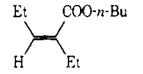
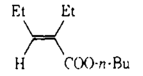
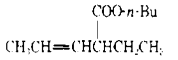
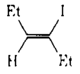
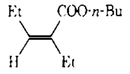
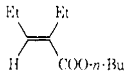
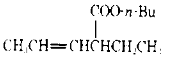
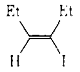
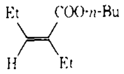
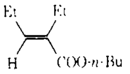
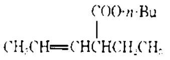
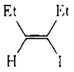
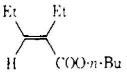
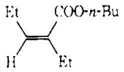
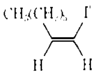
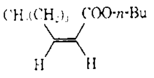
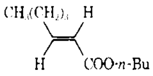
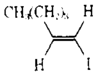
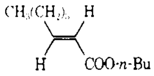
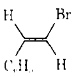
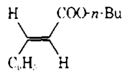
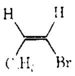
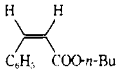
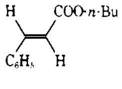
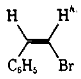
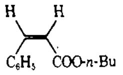
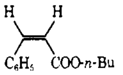
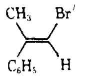
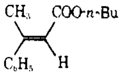
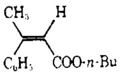
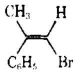
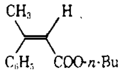
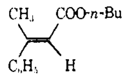
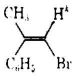
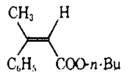
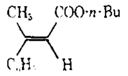
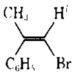
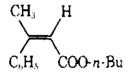
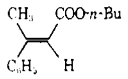
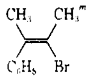
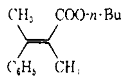
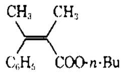
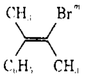
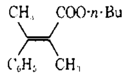
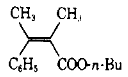
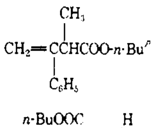
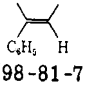
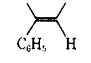
Halide	Catalyst	Temp, °C	Reaction time, hr	$\tau_{1/2}$, min	Products (% yield)	Bp, °C	Molecular weight Found	Molecular weight Calcd
 (16403-13-7)	$Pd(OAc)_2$	100	17	250	 (23) (52392-59-3)	50–55 (1.5 mm)	184.147[b]	184.146
					 (29) (52392-60-6)		184.147[b]	184.146
					 $\mathrm{CH_3CH{=}CH\overset{\overset{COO\text{-}\mathit{n}\text{-}Bu}{\vert}}{C}HCH_2CH_3}$ (21) (52392-61-7)		184.147[b]	184.146
 (23523-32-2)	$PdI_2(PPh_3)_2$	100	4.5	38	 (45)	60–68 (3 mm)		
					 (13)			
					 $\mathrm{CH_3CH{=}CH\overset{\overset{COO\text{-}\mathit{n}\text{-}Bu}{\vert}}{C}HCH_2CH_3}$ (24)			
 (16403-09-1)	$PdI_2(PPh_3)_2$	100	4.5	86	 (11)			
					 (69)[b]			
					 $\mathrm{CH_3CH{=}CH\overset{\overset{COO\text{-}\mathit{n}\text{-}Bu}{\vert}}{C}HCH_2CH_3}$ (19)[b]			
	$PdI_2(PPh_3)_2$	60	40	575	 (74)			
					 (6)			
 (16538-47-9)	$PdI_2(PPh_3)_2$	80	1.5	34	 (79) (52392-62-8)	66–69 (14 mm)	184.146	184.147
					 (6)			
 (16644-98-7)	$PdI_2(PPh_3)_2$	100	2	35	 (83) (52392-63-9)	74–78 (15 mm)	184[e]	184
 (588-72-7)	$PdBr_2(PPh_3)_2$	100	8	116	 (80) (52392-64-0)	155–165 (13 mm)[f]	204.102	204.115
 (588-73-8)	$PdBr_2(PPh_3)_2$	80	15	350	 (52)(53)[g] (52392-65-1)	90–94 (0.2 mm)	204.104	204.115
					 (30)(33)[g]			

Table II
(Continued)

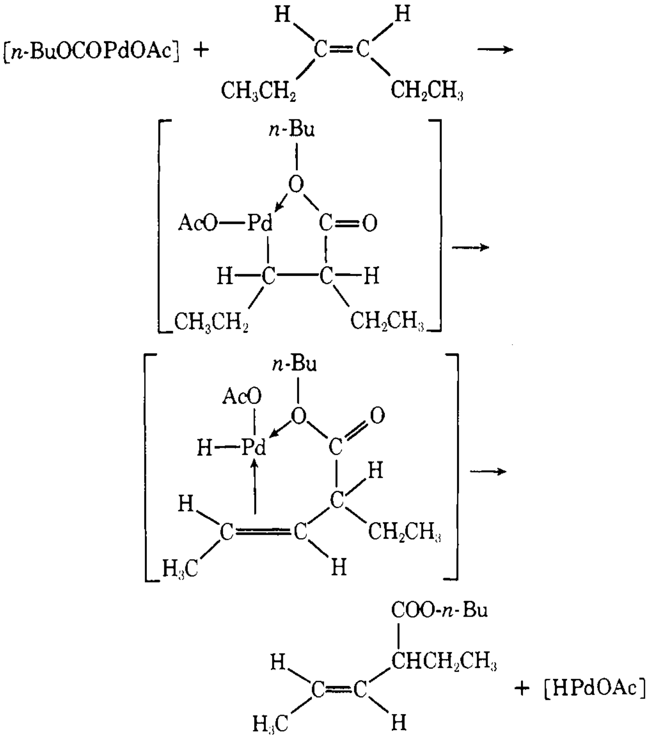
Halide	Catalyst	Temp, °C	Reaction time, hr	$\tau_{1/2}$, min	Products (% yield)	Bp, °C	Molecular weight	
							Found	Calcd
	$PdBr_2(PPh_3)_2$	60	43		 (68)	96–104 (0.2 mm)		
					 (16)			
 (16917-35-4)	$PdBr_2(PPh_3)_2$	125 ± 5			 (83) (52392-66-2)	108–112 (0.7 mm)		
					 (7) (52392-67-3)			
 (19647-26-8)	$PdBr_2(PPh_3)_2$	100	44	130	 (58)	90–108 (0.4 mm)	218.1295	218.1307
					 (33)		218.1297	218.1307
	$PdBr_2(PPh_3)_2$	100	150	3000	 (50)			
					 (4)			
	$PdBr_2(PPh_3)_2$	100	7		 (69)			
					 (26)			
 (52392-57-1)	$PdBr_2(PPh_3)_2$	100	168[n]	~1700	 (29) (52392-68-4)		232.1512	232.1463
					 (38) (52392-69-5)		232.1519	232.1463
 (52392-58-2)	$PdBr_2(PPh_3)_2$	100	168[o]	~1500	 (61)			
					 (7)			
					 $CH_2{=}\underset{C_6H_5}{C}\overset{CH_3}{C}HCOO\text{-}n\text{-}Bu^p$ (5)			
 (98-81-7)	$PdBr_2(PPh_3)_2$	100	5	70	 (68) (15895-94-0)	90–105 (1.5 mm)	204.105	204.115

[a] Carried out with 17.2 mmol of vinylic halide, 0.25 mmol of catalyst, 21.2 mmol of *n*-butyl alcohol, and 19 mmol of tri-*n*-butylamine at 1 atm of CO except where noted. [b] Samples isolated by glc. [c] Data corrected for 18% trans and 8% unknown in cis iodide. [d] Data corrected for 4% cis and 4% unknown in trans bromide. [e] Parent peak was too weak to be used to obtain a more accurate value. [f] Reported bp 162° (12 mm), G. H. Jeffery and A. I. Vogel, *J. Chem. Soc.*, 658 (1948). [g] Yields obtained under 30 psi pressure of carbon monoxide. [h] Reaction carried out at 20–30 psi of carbon monoxide. [i] Data corrected for 7% trans isomer in cis bromide. [j] Carried out under 1025 psig of CO. [k] Carried out with one-half quantities of reagents with an additional 2.5 mmol of triphenylphosphine added. [l] Carried out under an initial 1270 psig of CO with one-half quantities of reagents. [m] Carried out with 4 mmol of vinylic halide, 0.06 mmol of catalyst, 5 mmol of *n*-butyl alcohol, and 4.4 mmol of tri-*n*-butylamine at 1 atm of CO. [n] About 13% of unreacted starting bromide remained at this time. [o] About 15% of unreacted starting bromide remained at this time. [p] Isomeric structure not certain.

rapidly than the *Z* isomer does judging by the half-lives determined. In addition to the *E*- and *Z*-*n*-butyl 3-hexene-3-carboxylates, *n*-butyl 4-hexene-3-carboxylate was formed (probably trans but not definitely established). The identification of the third isomer was made from its nmr spectrum, its molecular weight, and the fact that it is obtained as the major product when "carbobutoxypalladium acetate" is treated with either *Z*- or *E*-3-hexene at 0–25°. The last reaction is similar to one reported previously between "carbomethoxypalladium acetate" and 1-hexene where a mixture of products composed of 42% *E*-methyl 2- and 58% methyl 3-heptenoate was formed.[13] The "carboalkoxypalladium acetates" were prepared by exchange reactions of palladium(II) acetate with carboalkoxymercuric acetates, obtained from alcohols, CO, and mercuric acetate by the method of Schoeller, *et al.*[14] In the 3-hexene reactions the α-substituent appears to be responsible for the formation of the ester as the major product. This result supports the idea that coordination of the palladium atom to the carboalkoxyl group in the alkylpalladium intermediate complex occurs and that this complex undergoes metal hydride elimination exocyclically to give the least strained olefin π-complex. The π-complex then dissociates into unsaturated ester and "hydridopalladium acetate" which itself then decomposes into palladium metal and acetic acid.[15] The α-ethyl group, by an entropy effect, would be expected to relatively favor the chelated form of the complex over the open chain solvated form. The starting olefins and product esters are stable under the reaction conditions. *Z*-3-Hexene gave 25%, and *E*-3-hexene 44% of *n*-butyl 4-hexene-3-carboxylate. The remainder of the products from *Z*-3-hexene were not the *E*- or *Z*-3-hexene-3-carboxylate but other materials, probably enol and allylic acetates and dicarboxylated products which were not identified. The *E*-3-hexene produced 6% of the *E*-3-hexene-3-carboxylate also but no *Z* ester, as expected by the normal cis addition–cis elimination mechanism believed to operate in the reaction.[13]

$$n\text{-BuOH} + \text{CO} + \text{Hg(OAc)}_2 \xrightarrow[30\text{ psi}]{25°} n\text{-BuOCOHgOAc} + \text{HOAc}$$

$$n\text{-BuOCOHgOAc} + \text{Pd(OAc)}_2 \longrightarrow [n\text{-BuOCOPdOAc}] + \text{Hg(OAc)}_2$$

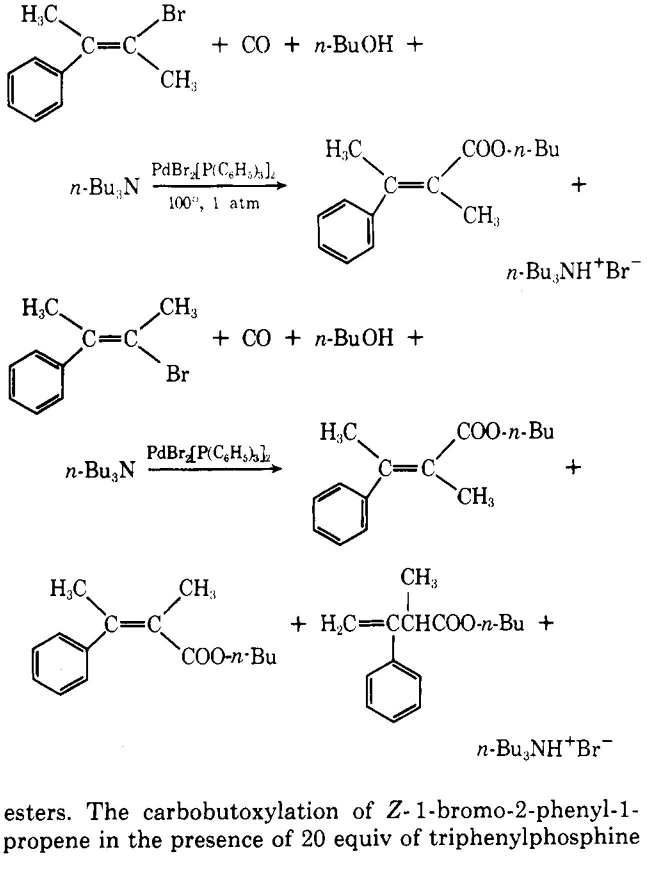


$$[\text{HPdOAc}] \longrightarrow \text{HOAc} + \text{Pd}$$

The formation of the nonconjugated ester from the carbobutoxylation of the 3-iodo-3-hexenes is quite sensitive to reaction temperature and this product disappears completely when the reactions are carried out at 60° rather than 100°. The relative amount of ester with retained configuration also increased on lowering the reaction temperature. Thus at 60° *E*-3-iodo-3-hexene gives 74% of the *E* carbobutoxylated product, only 6% of the *Z* isomer, and none of the nonconjugated ester compared with 69, 11, and 19%, respectively, at 100°.

The carbobutoxylations of both isomeric 3-iodo-3-hexenes were also carried out in hydroxyl deuterated *n*-butyl alcohol with diiodobistriphenylphosphinepalladium as catalysts in order to gain more information on how these reactions were occurring. In all cases, no mechanistically significant conclusions could be reached since all three isomeric ester products obtained were 50–75% monodeuterated under the reaction conditions. The results are shown in Table IV.

Z-1-Iodo-1-hexene on carbobutoxylation at 80° gave 79% *Z* and 6% *E* ester while the *E* iodide even at 100° gave only the *E* ester, which was isolated in 83% yield. Similarly *E*-2-bromostyrene at 100° gave only *E* *n*-butyl cinnamate, isolated in 80% yield. *Z*-2-Bromostyrene on the other hand at 80° gave 52% *Z* and 30% *E* ester while at 60° the yields were 68 and 16%, respectively. Increasing the CO pressure from atmospheric pressure to 30 psi did not improve the stereochemistry of the *Z*-2-bromostyrene reaction at 80°. Starting materials and products were stable under the reaction conditions.



The *E*- and *Z*-1-bromo-2-phenyl-1-propene isomers were carbobutoxylated with the results that the *E* bromide gave about 83% of the *E* ester (retention) and 7% of the *Z* ester and the *Z* bromide gave a mixture 33% *E* and 58% *Z* esters. The carbobutoxylation of *Z*-1-bromo-2-phenyl-1-propene in the presence of 20 equiv of triphenylphosphine per equivalent of $PdBr_2(PPh_3)_2$, on the other hand, led to a substantial improvement in the amount of ester obtained with retained structure, 92% compared with 64% without the excess phosphine under the same conditions. The reaction, however, was much slower with the excess phosphine. The carbobutoxylation under 1270 psig of carbon monoxide was only slightly more sterospecific than at atmospheric pressure (73% retention found *vs.* 64% at atmospheric pressure). Thus lowering reaction temperature or adding excess triarylphosphine are much more effective than increasing CO pressure in improving the stereochemistry of the carbobutoxylation. The *E*- and *Z*-2-bromo-3-phenyl-2-butenes isomers also were carbobutoxylated and the *E*-bromide gave mainly the *E* ester (61%) while the *Z*-bromide gave 38% *Z* and 29% *E* esters. A small amount of a new isomerie ester, presumably *n*-butyl 2-methyl-3-phenyl-3-butenoate was also formed in the *E*-bromide reaction.

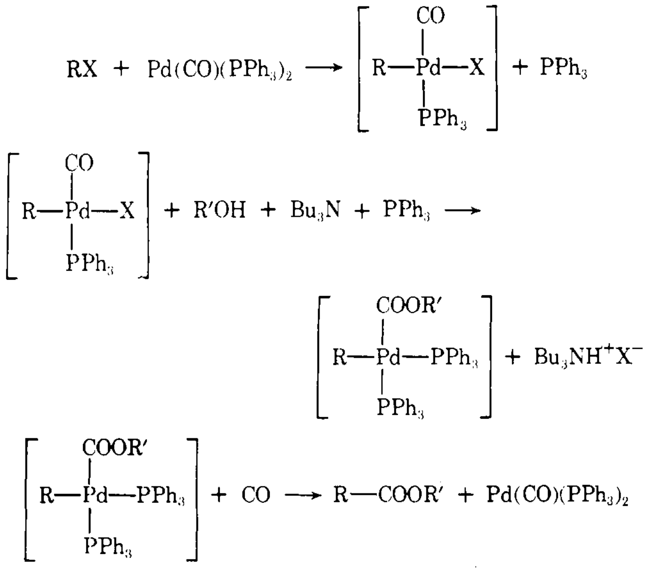
The carbobutoxylation of *E*- and *Z*-1-bromo-2-phenyl-1-propene was also carried out in hydroxyl deuterated *n*-butyl alcohol. In both the *E*- and *Z*-bromide reaction the ester produced with the opposite configuration to the starting bromide contained about 21–28% monodeuterated product while the esters with retained structures contained only about 10–14% monodeuterated product. Results are given in Table IV.

1-Bromostyrene was carbobutoxylated at 100° to give exclusively *n*-butyl 2-phenylacrylate which was isolated in 68% yield.

In an attempt to eliminate the toxicity problem encountered with nickel carbonyl in the catalytic halide carboxylation reported by Cassar and Foa[11] we tried the reaction with nonvolatile, dicarbonylbis(triphenylphosphine)nickel(0) as catalyst (5%). At 100° under 1 atm of carbon monoxide with iodobenzene no reaction occurred with only tri-*n*-butylamine present but carbobutoxylation did take place when sodium butoxide was added and *n*-butyl benzoate was formed in 68% yield (isolated) after 30 hr of reaction. This is an alternative method for the carboalkoxylation of halides if the reactants and/or products are not reactive toward sodium alkoxides at 100°. Tricarbonylmonophosphinenickel(0) complexes might be more reactive catalysts but these were not investigated.

Discussion of Results

At least two possible mechanisms of carboalkoxylation can be imagined. A reductive elimination of an aryl–carboalkoxypalladium species could be the final step in a mechanism such as the following



$$RX + Pd(CO)(PPh_3)_2 \longrightarrow \left[R\text{—}\overset{\displaystyle CO}{\underset{\displaystyle PPh_3}{Pd}}\text{—}X \right] + PPh_3$$

$$\left[R\text{—}\overset{\displaystyle CO}{\underset{\displaystyle PPh_3}{Pd}}\text{—}X \right] + R'OH + Bu_3N + PPh_3 \longrightarrow \left[R\text{—}\overset{\displaystyle COOR'}{\underset{\displaystyle PPh_3}{Pd}}\text{—}PPh_3 \right] + Bu_3NH^+X^-$$

$$\left[R\text{—}\overset{\displaystyle COOR'}{\underset{\displaystyle PPh_3}{Pd}}\text{—}PPh_3 \right] + CO \longrightarrow R\text{—}COOR' + Pd(CO)(PPh_3)_2$$

Since organopalladium compounds are known to undergo carbon monoxide "insertion reactions" very readily,[16] however, a more likely mechanism involves a CO insertion followed by attack of alcohol upon the acyl group with formation of a hydrido–palladium complex. The hydride then ultimately loses HX and reforms the catalyst.

$$RX + Pd(CO)[P(C_6H_5)_3]_2 \xrightarrow{-P(C_6H_5)_3} \begin{matrix} RPd(X)(CO)[P(C_6H_5)_3] \\ (\text{or } RPd(X)[P(C_6H_5)_3]_2) \end{matrix} \rightleftharpoons$$

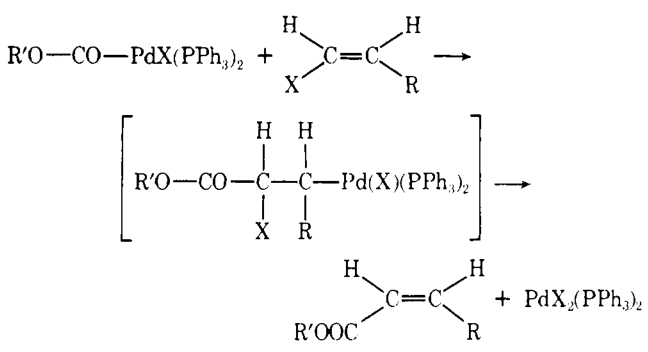
$$RCOPd(X)[P(C_6H_5)_3]_2 \xrightarrow{R'OH} RCOOR' + HPd(X)[P(C_6H_5)_3]_2$$

$$HPd(X)[P(C_6H_5)_3]_2 \underset{-CO}{\overset{CO}{\rightleftharpoons}} Pd(CO)[P(C_6H_5)_3]_2 + HX$$

$$HX + n\text{-}Bu_3N \longrightarrow n\text{-}Bu_3NH^+X^-$$

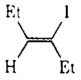
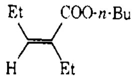
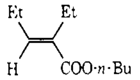
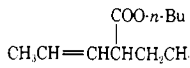
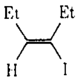
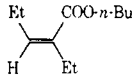
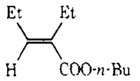
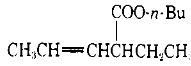
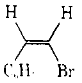
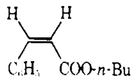
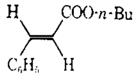
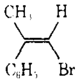
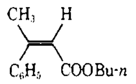
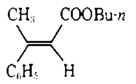
Presumably the vinylic halides and aryl halides react by the same mechanism. However, a possible cis-addition–trans-elimination mechanism with the vinylic halides could be imagined as shown below. This mechanism seems rather unlikely, however, since at least the tri- and tetrasubstituted vinylic halides which undergo this reaction, would not be expected to be very reactive to the addition of organopalladium compounds.[15]

$$PdX_2(PPh_3)_2 + R'OH + n\text{-}Bu_3N \longrightarrow R'OCOPd(X)(PPh_3)_2 + n\text{-}Bu_3NH^+X^-$$

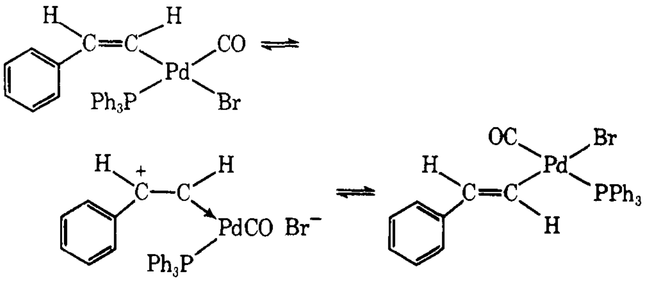


The means by which vinylic isomerization occurs in the carboalkoxylation is also of considerable interest. In all instances where the unsaturated esters produced contained the other geometric isomer than the starting vinylic halide, it was shown that the starting material and the products did not spontaneously isomerize under the reaction conditions. Furthermore, the ratio of isomerized to retained esters remained constant during the reactions. It is also clear that hydrogen groups are not required on the α- or β-vinyl carbon atoms in order for isomerization to take place. In examples where α- and/or β-hydrogens were present, reaction in hydroxyl deuterated *n*-butyl alcohol showed considerable incorporation of deuterium and some of it was at these positions. Clearly, cis–trans isomerization does not occur only by a palladium–hydride (deuteride) addition–elimination mechanism even in these cases. Probably, the isomerization occurs mainly in the σ-vinylic palladium intermediate before the CO insertion and alcoholysis occurs. It is not clear whether or not the CO insertion is reversible under our reaction conditions. A more than doubling of the CO pressure in the carbobutoxylation of *cis*-2-bromostyrene and increasing it by a factor of about 90 in the *Z*-1-bromo-2-phenyl-1-propene case did not greatly change the ratio of cis to trans-esters produced suggesting that the CO insertion is not reversible under our conditions. The loss of configuration at the vinylic palladium bond possibly is by way of an ionic carbene type intermediate such as the following.

Table IV
Carbobutoxylations with n-C_4H_9OD

Organic Halide[a]	Reaction temp, °C	$\tau_{1/2}$, min	Products (relative % yields)[b]		% Monodeuteration
	100	63		(47)	67
				(26)	55
			 $CH_3CH{=}CHCH(COO\text{-}n\text{-}Bu)CH_2CH_3$	(27)	75
	100	105		(8)	67
				(89)	80
			 $CH_3CH{=}CHCH(COO\text{-}n\text{-}Bu)CH_2CH_3$	(3)	49
	80	634		(52)	14
				(48)	21
	100	185		(59)	10
				(41)	28

[a] Reactants included 17.2 mmol of organic halide, 0.25 mmol of catalyst, 19 mmol of tri-n-butylamine, and 21.0 mmol of n-C_4H_9-OD. [b] Total yields were about the same as in the reactions with undeuterated n-butyl alcohol.



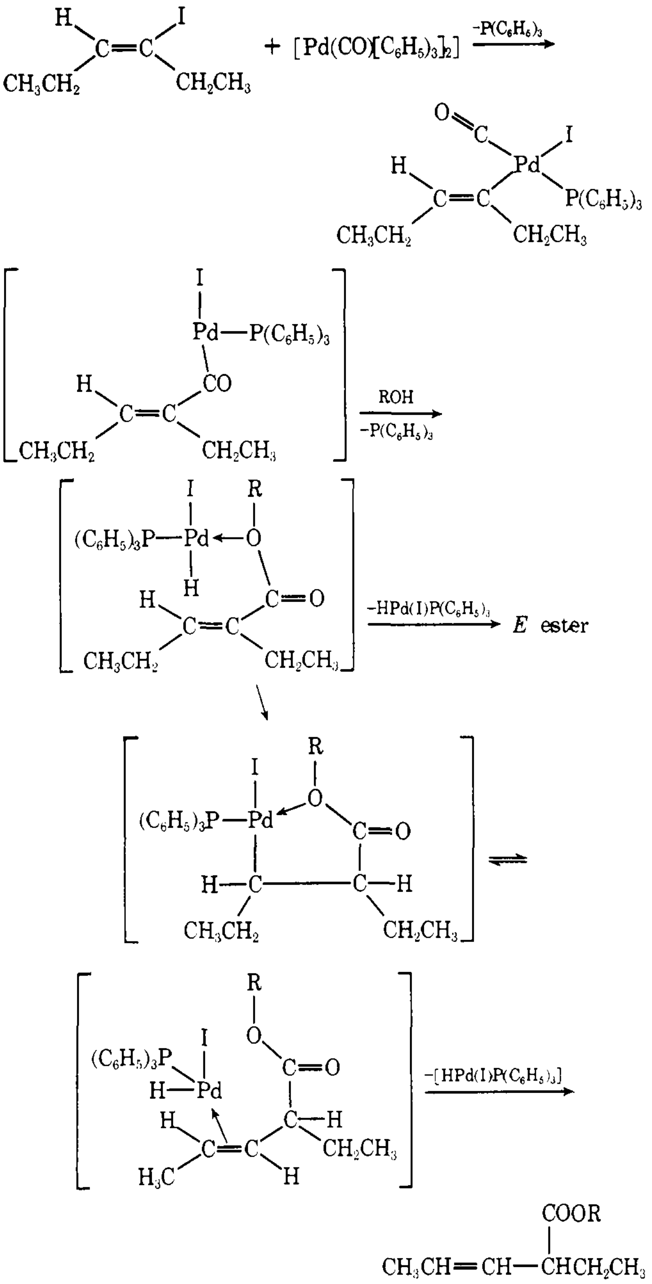
Excess triphenylphosphine may accelerate the CO insertion by forming a five coordinate intermediate and reduce the amount of carbene complex formed.[28]

The formation of β,γ-unsaturated esters in the E- and Z- 3-iodo-3-hexene carboalkoxylations may occur by a palladium hydride addition–elimination mechanism although attempts to establish this mechanism by looking for deuterium incorporation in this product when carbobutoxylation was carried out in hydroxyl deuterated n- butyl alcohol did not give conclusive results. As noted above all three of the isomeric esters produced were 50–80% deuterated. The nmr spectra of the glc separated ester products showed the deuterium was not concentrated at the vinylic positions. Presumably it was distributed over several positions, but we could not be certain from the spectra. A reasonable mechanism for formation of some of the β,γ-unsaturated ester can be proposed. In the synthesis of n- butyl 4-hexene-3-carboxylate from 3-hexene and n- carbobutoxypalladium acetate elimination to the β,γ-unsaturated ester was presumed to occur, as noted above, because of chelation of the palladium with the carboalkoxyl group during the elimination. Exactly the same chelated intermediate could be formed in the carbobutoxylation of the 3-iodo-3-hexenes if, after the alcoholysis step, the palladium hydride species formed remained coordinated to the ester group and then the hydride (deuteride) added internally to the existing double bond placing palladium on the β-carbon atom. Elimination of the chelated palladium hydride group exocyclically would form the 4-hexene-3-carboxylate ester.

The palladium hydride addition may occur in both directions and the elimination may produce a new isomer if a different hydride group is lost. In deuterated n- butyl alcohol such an isomerization would lead to deuterium incorporation and could account for the 10–15% excess deuterium found in the isomerized esters compared with the esters with retained configuration in the carbobutoxylations of E- and Z- 2-phenyl-1-bromo-1-propenes.

Another mechanism of formation of nonconjugated ester in the 3-iodo-3-hexene carbobutoxylation which needs to be considered is a π-allylic palladium hydride mechanism.[17] A control experiment using a mixture of the E- and Z- butyl 3-hexene-3-carboxylates under the carbobutoxylation conditions, however, failed to show the formation of any nonconjugated ester. Therefore, this ester must be formed directly by the reaction.

The palladium–triphenylphosphine catalyzed carboalkoxylation of aryl, benzylic, and vinylic halides appears to be a general reaction. The reaction with bromides and iodides occurs under mild and convenient conditions and is therefore a useful addition to the list of methods available for the synthesis of carboxylic acid esters.



Experimental Section

Reagents. Tri-*n*-butylamine (Eastman) was distilled from potassium hydroxide and stored over Linde 4A molecular sieves. Iodobenzene (Eastman) and *n*-butyl alcohol (Fisher Scientific) were distilled before use and also kept over molecular sieves. 1-Bromostyrene was prepared by the method of Glaser.[18] *E*-2-bromostyrene was used as obtained from the Aldrich Chemical Co. *Z*-2-Bromostyrene was prepared by the method of Cristol[19] and stored at 0°. *Z*- and *E*-1-bromo-2-phenyl-1-propene were prepared by the procedure of Davis and Roberts.[20] The isomeric mixture of bromides (33% *Z*) was separated by fractional distillation: *Z*-bromide, bp 86° (15 mm), and *E*-bromide, bp 96° (15 mm). *Z*-1-Iodo-1-hexene[21] and *E*-3-iodo-3-hexene[22] were also prepared by literature methods. *Z*-3-Iodo-3-hexene was prepared by refluxing 3-hexyne with constant boiling hydriodic acid for 24 hr, bp 43–44° (10 mm). Other organic halides except *Z*- and *E*-2-bromo-3-phenyl-2-butene (described below) were commercial products and were used without further purification.

Dichloro-, dibromo-, and diiodobis(triphenylphosphine)palladium(II) were prepared by heating potassium tetrachloropalladate with an excess of the potassium halide required and an excess of triphenylphosphine in ethanol solution.[23] The crude products were washed with water, ethanol, and pentane and then recrystallized from hot chloroform. Chlorobis(triphenylphosphine)phenylpalladium(II)[24] was prepared by the addition of the appropriate aryl halide to tetrakis(triphenylphosphine)palladium(0).[25] The bridged complex dibromo-$\mu\mu$-dibromobis(triphenylphosphine)palladium(II) was made by the addition of excess LiBr to equivalent amounts of K_2PdCl_4 and $Pd[C_6H_5)_3P]_2Cl_2$ in ethanol.[26] The bridged complex was then purified by recrystallization from chloroform.

Analysis. Samples were analyzed by gas chromatography on a 10 ft or a 15 ft 20% SE-30 on Chromosorb W column. If known samples were available, sensitivity coefficients were obtained compared with diphenyl ether. The diphenyl ether was then added as an internal standard. High resolution mass spectra were obtained by peak matching using a Du Pont (CED)21-110B double focus mass spectrometer. Infrared spectra were recorded on a Perkin-Elmer Model 337 grating spectrophotometer. Proton nuclear magnetic resonance spectra were measured with a Varian Associates Model A60A spectrometer or a Perkin-Elmer R-12B spectrometer using TMS as an internal standard.

***Z*- and *E*-2-Bromo-3-phenyl-2-butene.** To a stirred solution of 58.0 g (0.80 mol) of 2-butanone in 300 ml of ether at −78° in a 2-l. three-necked flask under argon was added 450 ml of 2.3 *M* phenyllithium in 70:30 hexane–benzene during 1 hr. The reaction mixture was allowed to stir at room temperature overnight. Ice water was then slowly added and the ether layer was separated, dried, and distilled. The crude 2-phenyl-2-butanol, bp 92–97° (11 mm), so obtained was then distilled with 10 g of sodium bisulfate at 11 mm. The crude olefin was redistilled to give a 41% yield of 2-phenyl-2-butene, bp 70–72° (12 mm).

To a stirred solution of 40 g of 2-phenyl-2-butene in 500 ml of chloroform at room temperature was slowly added 50 g of bromine in 200 ml of chloroform. After the addition, the chloroform was distilled from the product and a solution of 75 g of potassium hydroxide dissolved in 1 l. of ethanol was added. The solution was stirred at 55° for 1 hr and then water was added. The product was extracted with ether. The extracts were dried and distilled, bp 60–83° (0.7 mm). The isomeric mixture (38 g, 59%) was separated by fractionation. There was obtained 11.0 g (17%) of the *E*-bromide, bp 95–96° (14 mm) (nmr in $CDCl_3$, τ 2.55–3.10 (m, 5 H), 7.86 (s, 6 H); mol wt 209.9993, calculated 210.0045), and 6.0 g (9%) of the *Z*-bromide, bp 97–98° (14 mm) (nmr in $CDCl_3$, τ 2.80 (s, 5 H), 7.15 (q, 3 H, J = 1.5 Hz), 8.05 (q, 3 H, J = 1.5 Hz); mol wt 210.0015, calculated 210.0045). The structures of the bromides were established by treating each pure bromide with the tetramethylethylenediamine complex of *n*-butyllithium at 0° in ether and carboxylating with solid carbon dioxide. The bicarbonate soluble products were converted into the methyl esters with diazomethane and the samples were identified by comparison of their nmr spectra with those of the known isomeric methyl 2-methyl-3-phenyl-2-butenoates prepared by Jackman.[27]

General Procedure for the Carbonylation of Organic Halides. In a 100-ml jacketed flask containing a magnetic stirring bar was hung a Teflon cup containing 0.25 mmol of the palladium catalyst. The flask was then attached to a thermostated microhydrogenation-type apparatus.[12] The apparatus was flushed several times with carbon monoxide. The reagents, 17.2 mmol of the organic halide, 21.2 mmol of *n*-butyl alcohol, and 19.0 mmol of tri-*n*-butylamine, were injected into the reaction flask by means of a hypodermic syringe through a side arm provided with a stopcock and rubber septum on the end. The reaction vessel was then brought to the proper temperature (steam for 100° and circulating constant temperature bath for all other temperatures) and allowed to come to equilibrium at 1 atm of pressure. The Teflon cup containing the palladium catalyst was then dropped into the reaction mixture by means of a stopcock. Gas volume changes and times were periodically recorded until gas absorption stopped. The theoretical amount of 420 ml at 25° (17.2 mmol) was generally absorbed. The reaction mixture was then dissolved in ether and washed with several portions of 20% hydrochloric acid solution to remove salts and excess amine. The ether layer was washed with a saturated sodium bicarbonate solution followed by distilled water. The ether layer was dried with anhydrous magnesium sulfate, concentrated under reduced pressure, and then distilled *in vacuo* to give the pure esters.

Carbobutoxylations of Organic Halides with *n*-BuOD. Carbobutoxylations with n-C_4H_9OD (Aldrich, 98%) were carried out as described in the general procedure above. Samples for mass spectra were obtained by preparative glc on a 15 ft 20% SE-30 on Chromosorb W column. The ratio of deuterated to undeuterated organic ester was calculated from the intensity of the $(m + 1)/1$ peaks of the deuterated samples (average of three scans) minus the ratio of the intensity of the $(m + 1)/m$ peaks for the undeuterated samples. The results of the n-C_4H_9OD experiments are shown in Table IV.

***n*-Butyl *p*-Cyanobenzoate.** To a heavy-walled 200-ml Pyrex bottle was added 3.13 g (17.2 mmol) of *p*-bromobenzonitrile, 0.198 g (0.25 mmol) dibromobis(triphenylphosphine)palladium(II), and a magretic stirring bar. The bottle was capped with a rubber-lined metal cap with a small hole in it for injection by a needle and flushed with carbon monoxide several times through a needle and a mixture of 1.57 g (21.2 mmol) of *n*-butyl alcohol and 3.6 g (19.0 mmol) of tri-*n*-butylamine was injected into the bottle. The reaction mixture was placed in a steam bath, pressurized to 20 psi with CO and allowed to stir overnight (14 hr). The reaction mixture was then treated as above except that the product was crystallized from hexane rather than distilled to give 3.11 g (89% yield) of pure cyano ester.

Dicarbonylbis(triphenylphosphine)nickel(0) Catalyzed Carbobutoxylation of Iodobenzene. The same procedure was used as in the palladium catalyzed reaction above except that 5 mol % of dicarbonylbistriphenylphosphinenickel(0) (Alfa Chemical Co.) was used as catalyst and 26 ml of 1.5 *M* sodium *n*-butoxide in *n*-butyl alcohol was used in place of the amine and *n*-butyl alcohol.

Hydrogenation of the Products Obtained from the Carbobutoxylation of *trans*-3-Iodo-3-hexene. In a 45-ml high-pressure reactor was placed 0.75 g of the ester mixture, 7 ml of THF, and 0.25 g of platinum oxide. The reactor was sealed, cooled to −78° and flushed with nitrogen and then with hydrogen. The mixture was stirred magnetically in an oil bath at 60° under 1000 psi of hydrogen for 10 hr. Isolation of the product by dilution with water, extraction, and concentration and analysis by glc showed the reduction was incomplete. A 0.26-g sample of the partially hydrogenated product was rehydrogenated with 0.25 g of catalyst and 5 ml of THF at 100° under 1000 psi of hydrogen for 24 hr. Only a single product was present now which was isolated and identified as *n*-butyl 3-hexanecarboxylate by its nmr spectrum and its molecular weight as determined by mass spectroscopy. The parent ion was too weak to obtain a precise molecular weight but there was clearly a peak at 186 amu.

A new olefinic product was produced when hydrogenation was attempted at 60° under 1000 psi of hydrogen with 5% Pd-C as catalyst. This product judging by its nmr spectrum (from a small sample isolated by vpc) appeared to be *n*-butyl 2-hexene-3-carboxylate.

Carbobutoxymercuric Acetate. This compound was prepared essentially by the method of Schoeller, *et al.*[14] A solution of 6.37 g (20 mmol) of mercuric acetate in 25 ml of *n*-butyl alcohol was prepared in a 200-ml heavy-walled Pyrex bottle. The bottle was capped, flushed with carbon monoxide through a syringe needle through the self-sealing rubber lined cap, and stirred at room temperature under 50 psi of carbon monoxide for 2 days. The resulting mixture was filtered and cooled to 0°. The colorless solid which precipitated was separated by filtration and air-dried. There was obtained 5.51 g (77%) of the product.

Reactions of *Z*- and *E*-3-Hexene with "Carbobutoxypalladium Acetate." A mixture of 1.8 g (5 mmol) of *n*-carbobutoxymercuric acetate, 12 ml of acetonitrile, and 1 ml of the olefin was stirred in a ice bath and 1.15 g (5 mmol) of powdered palladium acetate was added. The mixture was then stirred overnight at room temperature. The products were analyzed by glc on a 15 ft 20% SE 30 on Chromosorb W column at 150° using diphenyl ether as an internal standard. The *Z*-3-hexene gave *n*-butyl 4-hexene-3-carboxylate in 25% yield with no other similar products formed while the *E*-olefin gave 44% of this ester and 6% *E*-*n*-butyl 3-hexene-3-carboxylate along with 14% of an unknown of longer retention time.

Relative Rate Measurements. The same general procedure as described above was employed except that half as much of each of the two halides whose relative rates were being measured was used. An internal standard of diphenyl ether was added. In the cases where two different organic halides were being compared, the catalyst used was half $PdBr_2[P(C_6H_5)_3]_2$ and half $PdI_2[P(C_6H_5)_3]_2$. Small samples (3–5 drops) of the reaction mixtures were withdrawn after about 5, 10, and 15% reaction had occurred judging by the gas absorbed. These samples were diluted with 10–15 drops of ether, washed with 5 drops of 20% hydrochloric acid and 5 drops of distilled water, and dried with anhydrous magnesium sulfate. After analysis by vpc, the data were plotted and linearly extrapolated back to zero time to obtain a more accurate value for the relative rates. The relative rates measured directly were the following: with palladium acetate alone as catalyst, *p*-iodoanisole was 1.1 times as reactive and *p*-bromobenzonitrile was 24 times as reactive as iodobenzene; with $PdX_2[P(C_6H_5)_3]_2$ catalysts, *p*-iodoanisole was 90 times as reactive, *p*-bromoanisole 0.23 times, and *p*-bromobenzonitrile 275 times as reactive as bromobenzene.

Acknowledgment. Support for this research was provided by the National Science Foundation, Grant No. GP-34492X1. Mass spectra were kindly determined by Dr. Barbara Jelus.

Registry No.—Carbon monoxide, 630-08-0; *n*-butyl alcohol, 71-36-3.

Supplementary Material Available. Full nmr data for the ester products described in this paper will appear in Table III following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche, referring to code number JOC-74-3318.

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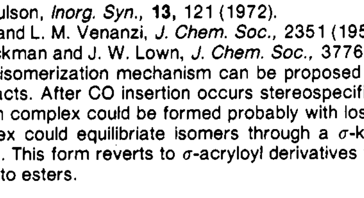
(28) Another isomerization mechanism can be proposed which also fits the known facts. After CO insertion occurs stereospecifically, a π-acryloylpalladium complex could be formed probably with loss of a ligand. Such a complex could equilibriate isomers through a σ-ketenemethylpalladium form. This form reverts to σ-acryloyl derivatives which ultimately alcoholize to esters.



An isolable π-acryloylcobalt complex has been reported previously [(R. F. Heck and D. S. Breslow, *J. Amer. Chem. Soc.*, **83,** 1097 (1961)] and a σ-ketenemethylcobalt species has been proposed to explain a trans- to cis-α,β-double bond isomerization in the thermal cyclization of tricarbonyltriphenylphospine-2,4-hexadienoylcobalt(I) [(R. F. Heck, *ibid.*, **85,** 3387 (1963)].