

CCl<sub>4</sub> or CDCl<sub>3</sub> as solvents, as specified, with Me<sub>4</sub>Si as the internal standard. Ultraviolet spectra were recorded with a Pye-Unicam SP-500 (series 2) spectrophotometer using spectroscopic-grade methanol. Mass spectra were obtained with either an AEI MS-702 or a JEOL DX-300 spectrometer operating at 70 eV. Melting and boiling points are uncorrected. TLC analyses and separations were carried out with SISCO silica gel. Petroleum ether refers to petroleum fraction boiling in the range 60–80 °C. Solvents used were purified and dried by standard procedures.

**Dialkyl Phosphorocyanidates 4a and 4b.** To a stirred suspension in benzene (50 mL) of finely powdered sodium cyanide (0.15 mol) and sodium hydroxide (0.005 mol) was added a solution of dialkyl phosphorochloridate (0.10 mol) in benzene (20 mL). After the addition was complete (15 min) the mixture was refluxed with stirring for 10 h. Filtration and removal of the solvent gave a reddish brown liquid. Distillation yielded a colorless liquid, which turned brown on standing. Redistillation after 10 weeks gave pure cyanidates **4a** and **4b**. Their IR spectra were identical with those of samples prepared by the reported procedure.<sup>5</sup>

**Dimethyl phosphorocyanidate (4a):** yield 30%; bp 90–91 °C (17 mm); IR (neat) 2200 ( $\nu_{\text{C}\equiv\text{N}}$ ); 1290 ( $\nu_{\text{P}=\text{O}}$ ); <sup>1</sup>H NMR (CCl<sub>4</sub>)  $\delta$  3.95 (d,  $J = 12$  Hz). Anal. Calcd for C<sub>3</sub>H<sub>6</sub>NO<sub>3</sub>P: C, 26.67; H, 4.44; N, 10.37. Found: C, 26.61; H, 4.08; N, 10.31.

**Diethyl phosphorocyanidate (4b):** yield 46%; bp 104–106 °C (14 mm) (lit.<sup>4</sup> bp 90–96 °C (14 mm)); IR (neat) 2200 ( $\nu_{\text{C}\equiv\text{N}}$ ), 1280 ( $\nu_{\text{P}=\text{O}}$ ); <sup>1</sup>H NMR (CCl<sub>4</sub>)  $\delta$  1.35 (t, 3 H), 4.12 (m, 2 H).

**Dialkyl (3-Aryl-1,2,4-oxadiazol-5-yl)phosphonates 6a–h and the Thiophosphonate 6i. General Procedure.** To a cooled (–5 to 0 °C) stirred solution of the cyanidates **4** (15 mmol) and the required arylhydroxamyl chloride<sup>20</sup> (15 mmol) in ether or THF (100 mL) was added triethylamine (15 mmol). After being stirred for 3–4 h at low temperature, the reaction mixture was kept overnight at room temperature, followed by heating under reflux for 0.5 h (water bath). Filtration and removal of the solvent gave light yellow to reddish oils.

All but three of the oxadiazoles were liquids that could be purified by fractional distillation. In all these cases an initial low-boiling fraction consisting of trialkyl phosphates was obtained. Two of the crystalline oxadiazoles (**6h** and **6i**) were obtained by triturating the oils with suitable solvents, while **6b** was obtained by preparative TLC (Table I; footnote b). They were crystallized from the solvents indicated in Table I. The mother liquor after the isolation of **6h**, on concentration and distillation under vacuum, yielded triethyl phosphate (**7b**) and in the case of **6i**, an analysis by GC showed the presence of triethyl thiophosphate (**7c**).

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In most cases the corresponding furoxans were either detected by TLC of the original reaction mixture or isolated and characterized by comparison with authentic samples.<sup>20,21</sup>

**Thermolysis of Phosphonates 6a and 6d.** Purified samples of each of the two systems (ca. 700 mg) were heated in a sealed tube placed in an oil bath. In the case of **6a** the temperature was maintained between 100 and 110 °C for 45 min, and in the case of **6d** it was maintained between 140 and 145 °C for 30 min. Kugelrohr distillation of the residues afforded trimethyl phosphate (**7a**, 58–60 °C (bath temperature) (3 mm); 10%, footnote c, Table I) from **6a** and triethyl phosphate (**7b**, 68–70 °C (bath temperature) (0.5 mm); 21%, footnote c, Table I) from **6d**; both were characterized spectroscopically.

**Thermolysis of 6a in the Presence of Acetophenone. Trapping of Monomeric Methyl Metaphosphate.** A reaction mixture consisting of the phosphonate **6a** (1.00 g), acetophenone (10 mL), and 2,2,6,6-tetramethylpiperidine (0.2 mL) was heated in a flask, protected from moisture, at 100 °C for 4 h. The resulting product was partitioned between CH<sub>2</sub>Cl<sub>2</sub> (100 mL) and 0.1 N NaOH (100 mL). The aqueous layer was extracted twice with 25-mL portions of CH<sub>2</sub>Cl<sub>2</sub> and concentrated in vacuo. The residual wine-red liquid was analyzed by TLC (CH<sub>3</sub>OH:CH<sub>3</sub>CN, 1:1, v/v). A band with  $R_f$  0.20–0.14 was extracted out with CH<sub>3</sub>OH–CH<sub>3</sub>CN. Removal of the solvent at reduced pressure yielded the enol phosphate **14** (25 mg;  $\approx$ 2%; footnote c, Table I): <sup>1</sup>H NMR (D<sub>2</sub>O; internal DSS)  $\delta$  3.45 (d, 3 H, <sup>3</sup>J<sub>P–H</sub> = 10 Hz; OCH<sub>3</sub>; lit.<sup>22</sup> 3.65, d, <sup>3</sup>J<sub>P–H</sub> = 10.8 Hz), 5.24 and 5.10 (two multiplets, each 1 H, H<sub>A</sub> and H<sub>B</sub> of vinylic group), 7.80–7.40 (m, 5 H, aromatic).

**Acknowledgment.** We express our sincere thanks to Dr. P. K. Ramachandran, Director, Defence R & D Establishment, Gwalior, for his keen interest and encouragement.

**Registry No.** **1a**, 813-77-4; **1b**, 814-49-3; **4a**, 3583-90-2; **4b**, 2942-58-7; **4c**, 87174-50-3; **5a**, 873-67-6; **5b**, 15500-74-0; **5c**, 49660-38-0; **5d**, 37737-65-8; **5e**, 13820-14-9; **5f**, 2574-03-0; **6a**, 87174-51-4; **6b**, 87174-52-5; **6c**, 87174-53-6; **6d**, 87174-54-7; **6e**, 87174-55-8; **6f**, 87174-56-9; **6g**, 87174-57-0; **6h**, 87174-58-1; **6i**, 87174-59-2; **7a**, 512-56-1; **7b**, 78-40-0; **7c**, 126-68-1; **14**, 87174-60-5; bis(4-nitrophenyl)furoxan, 31562-30-8; bis(2,4-dichlorophenyl)furoxan, 54696-53-6; acetophenone, 98-86-2.

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## Palladium-Catalyzed Conjugate Addition Type Reaction of Aryl Iodides with $\alpha,\beta$ -Unsaturated Ketones

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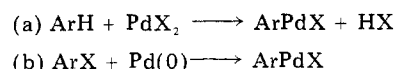
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Aryl iodides have been found to react with  $\alpha,\beta$ -unsaturated ketones in the presence of catalytic amounts of palladium, an excess of formic acid, and triethylamine, giving rise to conjugate addition type products. The electron-withdrawing power of the group attached to the olefinic double bond, the substituent  $\beta$  to the carbonyl group, and the basic reaction medium appear to affect greatly the conjugate addition/vinylic substitution ratio.

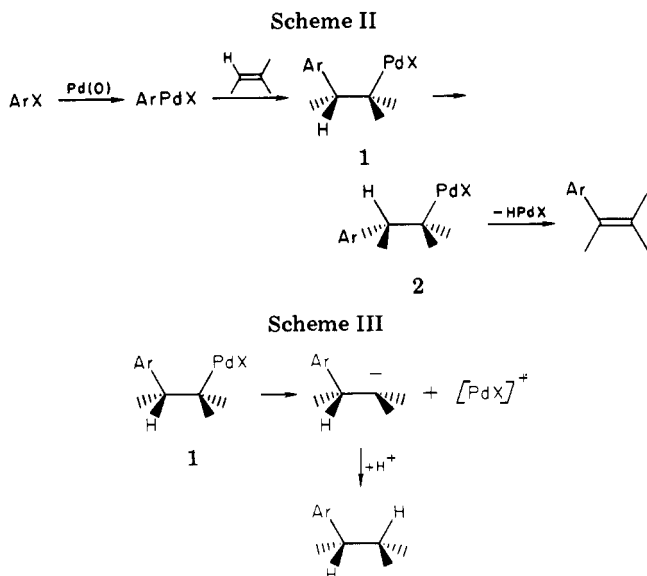
In previous papers<sup>1</sup> we have reported the reaction of arylmercury compounds with  $\alpha,\beta$ -enones in the presence of catalytic amounts of palladium(II) to give conjugate addition type products through in situ generated aryl-palladium intermediates. As arylmercury compounds can

### Scheme I



tolerate a wide variety of functional groups, the reaction allows an easy synthesis of  $\beta$ -aryl ketones and provides an improvement of the conjugate addition methodology. Unfortunately mercurials, even though usually high

(1) (a) Cacchi, S.; La Torre, F.; Misiti, D. *Tetrahedron Lett.* **1979**, 4591. (b) Cacchi, S.; Misiti, D.; Palmieri, G. *Tetrahedron* **1981**, **37**, 2941. (c) Cacchi, S.; Misiti, D.; Palmieri, G. *J. Org. Chem.* **1982**, **47**, 2995.



melting and relatively nonvolatile solids, are toxic compounds to be handled with care. When reactions are carried out on a laboratory scale, this problem may not be too serious. However, it could be a severe limitation when larger batches or industrial scale preparations are necessary. Therefore, it could be desirable to carry out an analogous palladium-catalyzed conjugate addition type reaction by using precursors of arylpalladium intermediates other than arylmercury compounds.

Focusing our attention on this problem, we looked at the alternative methods reported in the literature (Scheme I).

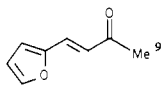

Arenes (Scheme Ia) did not appear suitable for our purposes because they produce arylpalladium intermediates through an electrophilic substitution reaction.<sup>2</sup> A lack of selectivity in the formation of a carbon-palladium bond when substituted benzenes are concerned is to be expected, thus giving rise to a variety of arylpalladium intermediates and consequently to a mixture of conjugate addition products.

Therefore, aryl halides (Scheme Ib) were selected as convenient arylpalladium precursors<sup>3</sup> and a study was undertaken to verify their involvement in a palladium-catalyzed conjugate addition type process. It is known that the reaction of palladium(0) complexes with aryl halides in the presence of olefinic double bonds results in the formation of vinylic substitution products<sup>4</sup> according to Scheme II.

It is apparent that this scheme would provide a new access to palladium-catalyzed conjugate addition type reactions if the intermediate derived from the addition of  $\text{ArPdX}$  to the olefinic double bond could be forced to undergo a  $\text{C}_\alpha\text{-Pd}$  heterolytic bond cleavage followed by protonation of the anionic moiety, as depicted in the Scheme III.

According to this scheme, palladium leaves the organic framework as a palladium(II) species, and to preserve a catalytic cycle it would be necessary to find conditions to achieve the reduction of Pd(II) species to Pd(0) species. This transformation has now actually been achieved, and aryl iodides have been found to react with  $\alpha,\beta$ -enones in the presence of catalytic amounts of Pd(0) species, formic acid, and triethylamine to give conjugate addition type

Table I. Palladium-Catalyzed Conjugate Addition Type Reaction of Phenyl Iodide with  $\alpha,\beta$ -Unsaturated Ketones<sup>a</sup>

entry	$\alpha,\beta$ -enone	reaction time, h	yield of 3, % <sup>b-d</sup>
a	$\text{PhCH=CHCOMe}$	5.5	60 (38)
b	$\text{PhCH=CHCOEt}^5$	6	59 (14)
c <sup>e</sup>	$\text{PhCH=CHCOCH}_2\text{Ph}^6$	5.5	61 (29)
d <sup>f</sup>	$\text{PhCH=CHCOPh}$	7	54 (36)
e	$\text{PhCH=CHCOCH=CHPh}^7$	6	37 <sup>g</sup> (10)
f	$\text{PhCH=CHCOC}_6\text{H}_4\text{-o-NO}_2^8$	6	22 (62)
g		6	21 (66)
h		7	40

<sup>a</sup> Unless otherwise noted, reactions were carried out under our usual conditions. <sup>b</sup> Reaction conditions were not optimized. Yields are calculated on the starting  $\alpha,\beta$ -enone and are given for isolated products. <sup>c</sup> Satisfactory C, H, and N analyses and IR spectra in agreement with the proposed structures were obtained. <sup>d</sup> Figures in parentheses refer to the recovered  $\alpha,\beta$ -enones. <sup>e</sup> The reaction was carried out with 0.2 mol % of  $\text{Pd(OAc)}_2(\text{PPh}_3)_2$ . <sup>f</sup> The reaction was carried out with 0.4 mol % of  $\text{Pd(OAc)}_2(\text{PPh}_3)_2$ . <sup>g</sup> 1,1,5,5-Tetraphenylpentan-3-one (3e'), derived from a double conjugate addition type reaction, was also isolated in 22% yield.

products in moderate to good yield. Now we wish to report the results obtained.

**Reaction of Phenyl Iodide with  $\alpha,\beta$ -Enones.** Using phenyl iodide as the phenyl donor, a variety of  $\beta$ -aryl ketones (3) has been obtained from the corresponding  $\alpha,\beta$ -enones.

The results are summarized in Table I.

The reaction variables have by no means been exhaustively studied, and considerable improvement in the yields may be possible. Even with the yields already obtained, however, the reaction is clearly a useful and convenient one for obtaining many conjugate addition products.

We have generally used about a 140 mol % excess of phenyl iodide, 164 mol % excess of formic acid, a 240 mol % excess of triethylamine, and 0.5 mol % of  $\text{Pd(OAc)}_2(\text{PPh}_3)_2$ , relative to the  $\alpha,\beta$ -enone. Of course, the reaction rates can be increased if more catalyst is used. Reactions were carried out on 3–4 mmol scale and  $\text{Pd(OAc)}_2(\text{PPh}_3)_2$  was selected instead of  $\text{Pd(OAc)}_2$  because, in the low scale runs we effected, it may be weighted more exactly. Palladium on charcoal could serve the purpose. However, we preferred to carry out reactions under homogeneous conditions. The addition of acetonitrile was found to be necessary to keep up the formed amine salt in solution. When the reaction was carried out without acetonitrile and with only an excess of triethylamine (Table III, entry f), crystallization of the salt from the reaction mixture blocked up the magnetic stirring well before the reaction could go to completion.

(5) Prepared in about 72% yield through a palladium-catalyzed vinylic substitution reaction (6 h) with phenyl iodide and pent-1-en-3-one under our usual conditions without formic acid: mp 38–40 °C; <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  7.78–7.18 (m, 6 H), 6.74 (B part of an AB system,  $J = 16.5$  Hz, 1 H), 2.67 (q,  $J = 7.5$  Hz, 2 H), 1.13 (t,  $J = 7.5$  Hz, 3 H).

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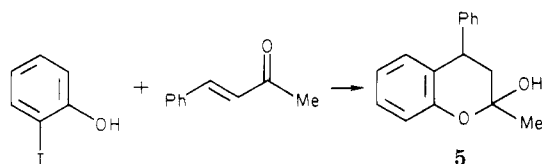
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**Table II. Palladium-Catalyzed Conjugate Addition Type Reaction of Aryl Iodides with Benzalacetone<sup>a</sup>**

entry	aryl iodides	reaction time, h	yield of 4, % <sup>b-d</sup>
a	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub> I	6	82 (12)
b	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> I	7	86
c	<i>p</i> -HOC <sub>6</sub> H <sub>4</sub> I	2	73
d	<i>p</i> -NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> I	2.5	43
e	<i>m</i> -HOCH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> I	7	79
f	<i>p</i> -MeCONHC <sub>6</sub> H <sub>4</sub> I	2	87
g	<i>m</i> -MeCONHC <sub>6</sub> H <sub>4</sub> I	5	67 (27)
h	<i>o</i> -MeCONHC <sub>6</sub> H <sub>4</sub> I	8	17 (77)
i	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> I	8	43 (36)
l	<i>m</i> -MeOCOC <sub>6</sub> H <sub>4</sub> I	5	31 (65)
m	<i>m</i> -HOCOC <sub>6</sub> H <sub>4</sub> I	7	50 (30) <sup>e</sup>

<sup>a</sup> Reactions were carried out under the usual reaction conditions. <sup>b</sup> Reaction conditions were not optimized. Yields are calculated on the starting benzalacetone and are given for isolated products. <sup>c</sup> Satisfactory C, H, and N analyses and IR spectra in agreement with the proposed structures were obtained. <sup>d</sup> Figures in parentheses refer to the recovered benzalacetone. <sup>e</sup> Not isolated; characterized as the methyl ester derivative 41. After workup, the yield was calculated from <sup>1</sup>H NMR analysis of the reaction mixture by using 4-methoxybenzophenone as the internal standard.

**Scheme IV**

Products derived from palladium-catalyzed olefinic double bond reduction,<sup>10</sup> vinylic substitution,<sup>4</sup> and coupling of aromatic moieties<sup>11</sup> were also isolated in low yield as well as major amounts of benzene.<sup>12</sup> Variable amounts of unreacted starting material were also recovered. As might be expected, phenyl bromide was found to be far less effective than phenyl iodide in participating in the conjugate addition path (under usual conditions, the conjugate addition product corresponding to benzalacetone was detected only in traces after 8 h).

**Reaction of Aryl Iodides with Benzalacetone.** The efficiency of this new route to  $\beta$ -arylated ketones was also tested by reacting a variety of aryl iodides with benzalacetone to give 4-aryl-4-phenylbutan-2-ones 4.

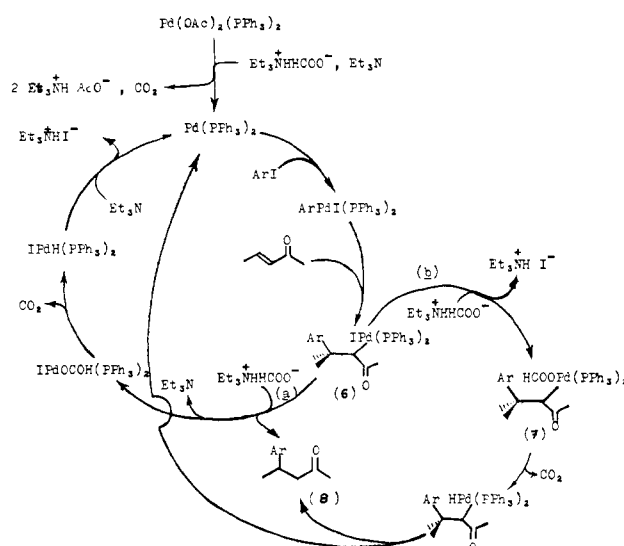
The results are summarized in the Table II.

As expected, the substituents in the aromatic ring affect the reaction rate. In addition, the presence of suitable nucleophiles in the ortho position may allow the conjugate addition product to undergo an in situ cyclization process. When we reacted benzalacetone with *o*-hydroxyiodobenzene under our usual conditions, 2-methyl-4-phenyl-2-chromanone (5) was isolated in about 30% yield.<sup>1c</sup>

It may be noted that addition products like that derived from *o*-(acetylamino)phenyl iodide (Table II, entry h) have been found to be useful intermediates in a new synthesis of the quinoline skeleton.<sup>13</sup>

### Discussion

Presumably, the conjugate addition type product does arise from the addition of the in situ formed  $\text{ArPdI}(\text{PPh}_3)_2$  to the olefinic double bond to give the intermediate 6

**Scheme V**

followed by  $\text{C}_\alpha$ -Pd heterolytic bond cleavage and protonation of the organic moiety (Scheme Va).

According to this scheme, formic acid is necessary to keep up the catalytic cycle through reduction of the rising Pd(II) species to Pd(0) species. Results obtained in the reactions carried out without the addition of formic acid (Table III, entries h and i) support this view.

The possibility that the conjugate addition product could arise from palladium-catalyzed reduction<sup>10</sup> of the vinylic substitution product was ruled out by the observation that, under usual GLC conditions, the reaction mixture was found to be free of 4,4-diphenylbutan-2-one when 4,4-diphenylbut-3-en-2-one was allowed to react in the presence of formic acid, triethylamine, and catalytic amounts of  $\text{Pd}(\text{OAc})_2(\text{PPh}_3)_2$  (the starting  $\alpha,\beta$ -enone was recovered in almost quantitative yield).

The presence of  $\text{ArPdCOH}(\text{PPh}_3)_2$  in a catalytic cycle similar to that shown in the Scheme Va should be also ruled out. When the reaction was carried out by using equimolar amounts of benzalacetone and phenyl iodide, after 1 h we found the phenyl iodide reacted completely to give benzene in about 90% yield (HPLC analysis); the addition product and benzalacetone were detected in about 7% yield and 91% yield, respectively.

This result clearly points out that decomposition of  $\text{PhPdCOH}(\text{PPh}_3)_2$  to benzene is faster than its addition to the olefinic double bond. It may be questionable, however, whether this result may represent the general behavior of intermediates of this kind; their reactivity can be very sensitive to substituent and solvent effects.

In the presence of the excess formic acid we have been using, the involvement of intermediate 7 (Scheme Vb) in a conjugate addition path is not inherently unlikely and cannot be excluded. Such an intermediate could be supposed to arise from replacement of iodide in the intermediate 6 by formate and to collapse to 8 through deinsertion of carbon dioxide and reductive elimination of the organic moiety. This reductive mechanism was proposed by Heck<sup>12</sup> to account for the palladium-catalyzed formation of arenes from aryl halides.

Whatever the real mechanism for decomposition of the intermediate derived from the addition of the in situ formed arylpalladium to the  $\alpha,\beta$ -enonic system may be, it remains that formic acid must play an important role in this range of the reaction coordinate.

Benzalacetone was recovered in about 80% yield when allowed to react under our usual conditions without formic

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Table III. Solvent, Catalyst, and Reducing Agent in the Reaction of Benzalacetone with Iodobenzene<sup>a</sup>

entry	catalyst	base	solvent	acid	products, % yield <sup>b</sup>			
					total yield, % <sup>b</sup>	starting material	conjugate addition	vinylc substitution
a	Pd(OAc) <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	Et <sub>3</sub> N	MeCN	HCOOH	97	34	61.9	4.1
b	Pd(OAc) <sub>2</sub>	Et <sub>3</sub> N	MeCN	HCOOH	95	25.3	68.4	6.3
c	Pd(5%)/C	Et <sub>3</sub> N	MeCN	HCOOH	94	28.7	64.9	6.4
d	Pd(OAc) <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	Et <sub>3</sub> N	DMF	HCOOH	91	17.6	78	4.4
e	Pd(OAc) <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	Et <sub>3</sub> N	DMSO	HCOOH	89	34.8	59.6	5.6
f <sup>c</sup>	Pd(OAc) <sub>2</sub>	Et <sub>3</sub> N		HCOOH	97	50.5	46.4	3.1
g	Pd(OAc) <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>		MeCN	HCOOH	92	100		
h	Pd(OAc) <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	Et <sub>3</sub> N	MeCN		91	87.8	9.9	2.3
i	Pd(OAc) <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub> <sup>d</sup>	Et <sub>3</sub> N	MeCN		83	5.2	62.3	32.5

<sup>a</sup> Unless otherwise noted reactions were carried out with 3.4 mmol of benzalacetone, 8.16 mmol of phenyl iodide, 11.56 mmol of triethylamine, 0.017 mmol of Pd(OAc)<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, and 1 mL of solvent at 80 °C for 6 h. <sup>b</sup> Percentages refer to single runs and are calculated on isolated products. <sup>c</sup> This reaction was carried out with 37 mmol of triethylamine. Crystallization of the ammonium salt blocked up the magnetic stirring after about 1 h. <sup>d</sup> This reaction was carried out (2 h) with 3.4 mmol of Pd(OAc)<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>.

acid (Table III, entry h). The vinylc substitution product was obtained in about 2% yield together with 9% yield of the conjugate addition product. This last value is far beyond the amount of the added palladium catalyst (0.5 mol %) and suggests at least three considerations: (a) The value of the conjugate addition/vinylc substitution ratio is dependent upon the presence of formic acid. When the reaction is carried out without the addition of formic acid, this value is lowered presumably because of the lack of the reducing step in the catalytic cycle (it may be remembered that the vinylc substitution reaction gives rise to Pd(0) species). (b) Under conditions very close to those largely reported in the literature<sup>4</sup> to allow vinylc substitution reactions to occur on a variety of alkenes,  $\alpha,\beta$ -unsaturated acids, esters, acetals and ketals of  $\alpha,\beta$ -unsaturated aldehydes and ketones, and allylic alcohols (in these last three cases the composition of the reaction mixture is strongly dependent on the direction of hydrogen elimination), benzalacetone (and other  $\alpha,\beta$ -enones; see Table I) shows a tendency to follow the conjugate addition pathway. This tendency is confirmed by the isolation of 4,4-diphenylbutan-2-one in 52% yield when benzalacetone was treated (2 h) with phenyl iodide in the presence of triethylamine, acetonitrile, and a stoichiometric amount of Pd(OAc)<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (Table III, entry i). (c) In the absence of formic acid, Pd(0) is still generated presumably through reduction of Pd(II) by triethylamine,<sup>11</sup> but this pathway is much less effective.

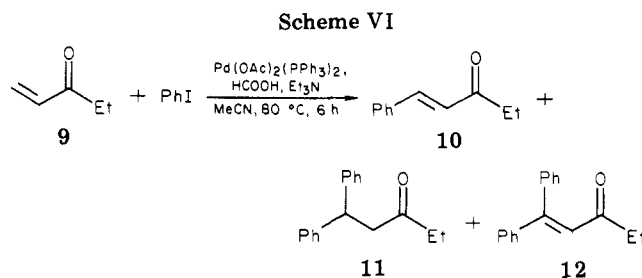
Clearly, competition between conjugate addition and vinylc substitution depends on a variety of factors affecting the reactivity of the intermediate 6, two of which can be recognized in both steric and electronic factors.

In what concerns steric effects, at least with the examples reported, it was found that variations in the steric demand of the substituents bonded to the carbonyl group (Table IV, entry a) or in the nature of the ligands of palladium (see Table III) do not alter significantly the conjugate addition/vinylc substitution ratio. On the contrary, the nature of the substituent at the  $\beta$ -carbon of the  $\alpha,\beta$ -enonic system can produce remarkable changes: more hindered groups tend to favor the conjugate addition path presumably through restriction in rotation around the C <sub>$\alpha$</sub> -C <sub>$\beta$</sub>  single bond necessary to attain the conformation required for syn elimination of HPdI.<sup>14</sup> A convincing example of how the substituent at the  $\beta$ -carbon may affect the reaction pathway is given by the reaction of pent-1-en-3-one (R = H) (Scheme VI).

Table IV. Relative Percentages<sup>a</sup> of Conjugate Addition and Vinylc Substitution Products<sup>b</sup>

entry	starting material	conjugate addition product, %	vinylc substitution product, %
a	$\alpha,\beta$ -enone (a-h; Table I)	93-98	2-7
b	PhCH=CHCHO	92	8
c	PhCH=CHCOOMe <sup>c</sup>	19	81
d	PhCH=CHCONH <sub>2</sub> <sup>c</sup>	23	77

<sup>a</sup> Relative percentages refer to single runs and are given on isolated products. <sup>b</sup> Cinnamaldehyde, methyl cinnamate, and cinnamamide were reacted for 6 h under the conditions described for the  $\alpha,\beta$ -enones. <sup>c</sup> Under our conditions methyl cinnamate and cinnamamide were found much less reactive than cinnamaldehyde and  $\alpha,\beta$ -enones.



When pent-1-en-3-one was treated with phenyl iodide under our usual conditions, compounds 10 and 11 were obtained in about 36% yield while compound 12 was detected only in traces (about 3%). These results can be accounted for by assuming that the  $\beta$ -unsubstituted  $\alpha,\beta$ -enonic system 9 reacts initially through the known vinylc substitution path; then, the in situ formed  $\beta$ -substituted  $\alpha,\beta$ -enonic system 10 reacts further to give selectively the conjugate addition derivative 11.

When this reaction was carried out (6 h) under the same conditions but without formic acid, compounds 10, 11, and 12 were obtained in about 72% yield, 10% yield, and 3% yield, respectively.

If we compare these results with those reported by Heck<sup>15</sup> in the reaction of methyl acrylate with phenyl iodide in the presence of catalytic amounts of Pd(0) (methyl acrylate was reported to produce methyl 3,3-di-

(14) Dieck, H. A.; Heck, R. F. *J. Am. Chem. Soc.* 1974, 96, 1133.(15) Cortese, A. N.; Ziegler, C. B., Jr.; Hrnjez, B. J.; Heck, R. F. *J. Org. Chem.* 1978, 43, 2952.

phenylacrylate in 70% yield through a double vinylic substitution) it becomes apparent that, in addition to steric effects of  $\beta$ -substituents, electronic effects related to the group attached to the olefinic double bond must also affect the conjugate addition/vinylic substitution ratio.

Generalization from the results reported in Table IV, concerning a variety of  $\alpha,\beta$ -unsaturated carbonyl systems, have to be drawn with caution; nevertheless, within experimental error, a trend can be recognized; i.e., an increase in the electron-withdrawing power tends to favor the formation of the conjugate addition product.

Last, but not least, the basic reaction medium seems to play a not negligible role in the competition between conjugate addition and vinylic substitution. With regard to this matter, it is noteworthy to compare the 75% yield of vinylic substitution product reported by Yamamura<sup>16</sup> in the reaction of chalcone with benzene and acetic acid in the presence of Pd(OAc)<sub>2</sub> with the 54% yield of conjugate addition product obtained in the reaction of chalcone under our conditions<sup>17</sup> (Table I, entry d).

In conclusion, competition between C<sub>α</sub>-Pd bond cleavage coupled with formation of the C<sub>α</sub>-H bond and syn elimination of HPdI appears to be dependent upon a complex balance of steric, electronic, and medium factors influencing the reactivity of the intermediate derived from the addition of ArPdI(PPh<sub>3</sub>)<sub>2</sub> to the olefinic double bond; none of them, at least with the examples reported, can direct the reaction to the formation of the conjugate addition type product by itself. However, no troublesome reaction conditions or particular constraints in the substrate are required to allow the conjugate addition to occur.

In spite of the apparent complexity, this palladium-catalyzed conjugate addition type reaction, as demonstrated in this paper, can be easily achieved with a variety of  $\alpha,\beta$ -enonic systems and aryl iodides and it holds promise as a useful synthetic method.

### Experimental Section

Melting points are uncorrected and were determined with a Büchi apparatus.

All of the reagents, solvents, and catalysts commercially available were used as received without further purification.  $\alpha,\beta$ -Enones **b,c,e,f,g** were prepared as reported. (Acetyl-

amino)phenyl iodides **f,g,h** and 3-carbomethoxyphenyl iodide **l** were prepared from commercially available anilines and carboxylic acid through standard methods.

The products were purified on axially compressed columns (Chromatospac Prep 10 or Miniprep from Jobin Yvon) packed with LiChroprep Si-60 15–25  $\mu$  (Merck) by eluting with *n*-hexane/ethyl acetate mixtures. The solvent delivery system and the refractive index detector were from Waters (PrepLC/System 500A).

<sup>1</sup>H NMR spectra (measured in CDCl<sub>3</sub> with Me<sub>4</sub>Si as an internal standard) and mass spectra (70 eV) were recorded with a Varian EM390 spectrometer and a Hewlett-Packard HP 5980A spectrometer equipped with a Hewlett-Packard Data System 5934A.

**General Procedure for Palladium-Catalyzed Conjugate Addition Type Reaction of Aryl Iodides with  $\alpha,\beta$ -Unsaturated Carbonyl Compounds.** The starting  $\alpha,\beta$ -unsaturated carbonyl compound (3.4 mmol) was added to a mixture of aryl iodide (8.16 mmol) and triethylamine (11.56 mmol). Then, Pd(OAc)<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (0.017 mmol) and acetonitrile (1 mL) were added. The mixture was gently purged with argon, and formic acid (8.97 mmol) was added all at once. The mixture was stirred at 80 °C under argon atmosphere for an appropriate period, AcOEt and water were added, and the organic layer was separated, washed with water, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated under reduced pressure. The residue was filtered through a short bed of Florisil (elution with *n*-hexane/AcOEt mixtures), concentrated, and chromatographed through preparative HPLC.

**Registry No.** **4** (Ar = *p*-MeC<sub>6</sub>H<sub>4</sub>), 80331-24-4; **4** (Ar = *p*-MeOC<sub>6</sub>H<sub>4</sub>), 76217-07-7; **4** (Ar = *p*-HOC<sub>6</sub>H<sub>4</sub>), 80331-29-9; **4** (Ar = *p*-NH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>), 87351-06-2; **4** (Ar = *m*-HOCH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>), 87351-07-3; **4** (Ar = *p*-MeCONHC<sub>6</sub>H<sub>4</sub>), 80331-30-2; **4** (Ar = *m*-MeCONHC<sub>6</sub>H<sub>4</sub>), 87351-08-4; **4** (Ar = *o*-MeCONHC<sub>6</sub>H<sub>4</sub>), 87351-09-5; **4** (Ar = *p*-ClC<sub>6</sub>H<sub>4</sub>), 29869-86-1; **4** (Ar = *m*-MeOCOC<sub>6</sub>H<sub>4</sub>), 80331-27-7; **4** (Ar = *m*-HOCOC<sub>6</sub>H<sub>4</sub>), 80331-28-8; **10**, 3152-68-9; **11**, 87351-01-7; PhCH=CHCOMe, 122-57-6; PhCH=CHCOCH<sub>2</sub>Ph, 5409-59-6; PhCH=CHCOPh, 94-41-7; PhCH=CHCOCH=CHPh, 538-58-9; PhCH=CHCOC<sub>6</sub>H<sub>4</sub>*o*NO<sub>2</sub>, 16619-38-8; Ph<sub>2</sub>CHCH<sub>2</sub>COMe, 5409-60-9; Ph<sub>2</sub>CHCH<sub>2</sub>COCH<sub>2</sub>Ph, 87351-02-8; Ph<sub>2</sub>CHCH<sub>2</sub>COPh, 606-86-0; Ph<sub>2</sub>CHCH<sub>2</sub>COCH<sub>2</sub>CHPh<sub>2</sub>, 87351-03-9; Ph<sub>2</sub>CHCH<sub>2</sub>COC<sub>6</sub>H<sub>4</sub>*o*NO<sub>2</sub>, 87351-04-0; *p*-MeC<sub>6</sub>H<sub>4</sub>I, 624-31-7; *p*-MeOC<sub>6</sub>H<sub>4</sub>I, 696-62-8; *p*-HOC<sub>6</sub>H<sub>4</sub>I, 540-38-5; *p*-NH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>I, 540-37-4; *m*-HOCH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>I, 57455-06-8; *p*-MeCONHC<sub>6</sub>H<sub>4</sub>I, 622-50-4; *m*-MeCONHC<sub>6</sub>H<sub>4</sub>I, 19230-45-6; *o*-MeCONHC<sub>6</sub>H<sub>4</sub>I, 19591-17-4; *p*-ClC<sub>6</sub>H<sub>4</sub>I, 637-87-6; *m*-MeOCOC<sub>6</sub>H<sub>4</sub>I, 618-91-7; *m*-HOCOC<sub>6</sub>H<sub>4</sub>I, 618-51-9; Pd(OAc)<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, 14588-08-0; Pd(OAc)<sub>2</sub>, 3375-31-3; Pd, 7440-05-3; 4-(2-furanyl)-3-buten-2-one, 623-15-4; 2-cyclohexen-1-one, 930-68-7; 4-(2-furanyl)-4-phenylbutan-2-one, 87351-05-1; 3-phenylcyclohexan-1-one, 20795-53-3; phenyl iodide, 591-50-4; benzalacetone, 122-57-6.

**Supplementary Material Available:** Melting points, <sup>1</sup>H NMR, and MS data of addition products **3** and **4** (4 pages). Ordering information is given on any current masthead page.

(16) Yamamura, K. *J. Org. Chem.* **1978**, *43*, 724.

(17) We have observed the same pattern for benzalacetone: the vinylic substitution product was obtained in 73% yield when treated with benzene, acetic acid, and Pd(OAc)<sub>2</sub> while the addition product was obtained in 60% yield under our usual conditions.