Palladium-Catalyzed Heck Arylations of Allyl Alcohols in Ionic Liquids: Remarkable Base Effect on the Selectivity

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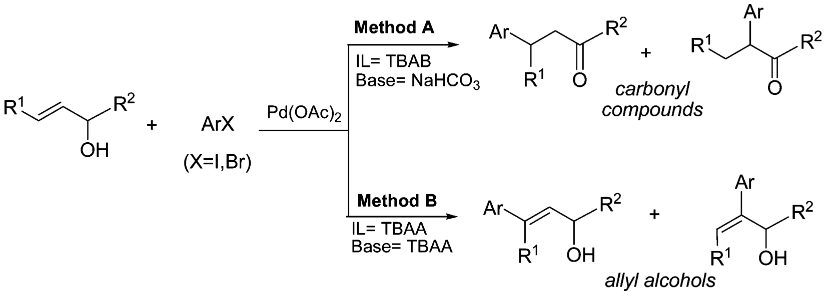
Received January 2, 2007



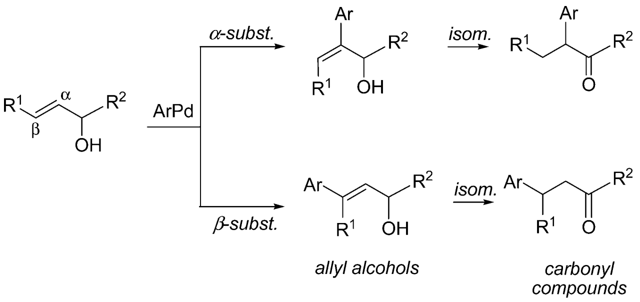
Pd-catalyzed Heck arylation of allyl alcohols in tetraalkylammonium ionic liquids (ILs) can be made highly selective toward the formation of either aromatic carbonyl compounds or aromatic conjugated alcohols by carefully choosing both the IL and the base.

Introduction

The palladium-catalyzed Heck arylation of olefins is one of the most powerful methods for the formation of C−C bonds.[1] This process is generally applied to electron-deficient alkenes; otherwise, reactions are sluggish and mixtures of regioisomeric olefins are formed, thus making the method of only limited synthetic utility. When allyl alcohols are used as substrates, the problem with the selectivity is further complicated by the formation of carbonyl products via isomerization of the initially formed arylated allyl alcohols, so much that four arylated products can be obtained (Scheme 1).[2]

The regioselectivity of the insertion is mainly controlled by steric factors; indeed, with terminal alkenols ($R^1 = H$), the addition of the aryl moiety usually occurs on the unsubstituted carbon of the double bond with few exceptions.[3] With internal olefins ($R^1 \neq H$) also other factors can play a role such as the coordination properties of the hydroxyl group or the effect of the base,[4,5] and selectivity seems to be quite unpredictable depending on the reaction conditions.

SCHEME 1. General Trend in the Heck Arylation of Allyl Alcohols



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(3) See for example (a) Mo, J.; Xu, L.; Ruan, J.; Liu, S.; Xiao, J. *Chem. Commun.* **2006**, *34*, 3591−3593. (b) Pei, W.; Mo, J.; Xiao, J. *J. Organomet. Chem.* **2005**, *690*, 3546−3551.

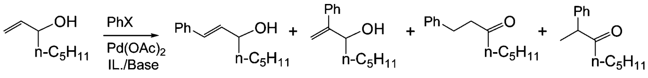
10.1021/jo070005f CCC: $37.00

Much less studied is the isomerization process, which impedes the arylated allylic alcohols to be isolated. Indeed, only few examples have been reported showing the substitution of allylic alcohols by aryl halides occurring without the isomerization of the double bond. In these cases, special additives such as silver salts,[6] cesium carbonate,[7] or unusual substrates such as aryl triflates[8] and hypervalent iodonium salts[4] proved to be necessary. Because of the synthetic importance of both conjugated aromatic alcohols and the corresponding carbonyl compounds, the development of a method which allows to control the isomerization process would be of significant utility.

In a program aimed at developing powerful catalytic methods in ionic liquids (ILs),[9] we disclosed that highly efficient Heck olefinations of aryl halides can be accomplished in tetraalkylammonium ILs, obviating the need for toxic solvents and labile phosphane ligands.[1d,10] In particular, some ILs such as tetrabutylammonium bromide (TBAB) and tetrabutylammonium acetate (TBAA) proved to be exceptionally able to stabilize colloidal palladium nanoparticles that in these media act as very active and selective catalysts for the C−C couplings. As an example, the Heck arylation of cinnamates[11] can be performed in a high stereoselective manner thanks to the aptitude of TBAA to rapidly neutralize the Pd−H species responsible for the *E*/*Z* isomerization.

Results presented below fall again in line with this hypothesis, showing that a comparable control on the selectivity can also be reached with allyl alcohols, avoiding the need for aryl triflates or toxic and costly inorganic additives.

TABLE 1. Base Effect on the Heck Arylation of 1-Octen-3-ol Catalyzed by Pd(OAc)$_2$[a]



1a **1b** **1c** **1d**

run	X	IL	base	*T* [˚C]	*t*/*h*	convn[b] (%)	yields[c] (%)	ratio (%)[b] **1a**/**1b**/**1c**/**1d**
1	I	TBAB	$NaHCO_3$	110	2.5	>99	89	0/0/97/3
2	I	TBAB	K_2CO_3	110	1	>99	92	0/0/94/6
3	I	TBAB	Bu_3N	110	1.5	>99	91	0/0/94/6
4	I	TBAB	NaOAc	110	3.5	>99	85	0/0/95/5
5	Br	TBAB	$NaHCO_3$	130	3	>99	90	0/0/94/6
6	Br	TBAB	K_2CO_3	130	1	>99	93	0/0/94/6
7	Br	TBAB	Bu_3N	130	12	55	45	0/0/95/5
8	Br	TBAB	NaOAc	130	12	62	49	0/0/95/5
9	Br	TBAB	TBAA	90	0.7	>99	90	48/9/43/0
10[d]	Br	TBAB	TBAA	90	0.5	>99	92	56/10/34/0
11[e]	Br	TBAB	TBAA	90	0.5	>99	93	65/10/25/0
12	Br	TBAA	TBAA	90	0.5	>99	90	85/4/11/0
13	Br	TBAA	TBAA	80	0.5	>99	90	86/3/11/0
14	Br	TBAA	TBAA	70	0.5	>99	94	90/6/4/0
15	Br	TBAA	TBAA	60	1.5	>99	85	83/5/11/0
16	Br	TBAA	TBAA	50	14	<1		
17	I	TBAA	TBAA	80	1	>99	93	85/5/10/0
18	I	TBAA	TBAA	70	2	>99	90	85/11/4/0
19	I	TBAA	TBAA	60	1.5	96	89	80/12/8/0
20	I	TBAA	TBAA	rt	2.5	93	85	65/16/19/0

[a] General reaction conditions: IL (1 g), halobenzene (1.2 mmol), allyl alcohol (1 mmol), Pd(OAc)$_2$ (1.2 mol %); base (2 mmol or 1 g of TBAA when it was used as both base and IL), TBAA/TBAB = 1:1.5 (mmol ratio). [b] Conversions and product ratios evaluated by ^{1}H NMR. [c] Isolated overall yields. [d] TBAA/TBAB = 1.5:1 (mmol ratio). [e] TBAA/TBAB = 4:1 (mmol ratio).

Results and Discussion

Recently, we reported[12] an efficient Heck arylation of allyl alcohols carried out in molten TBAB catalyzed by a Pd−benzothiazole−carbene complex using $NaHCO_3$ as base. Reactions followed the usual pathway of the Heck coupling with allyl alcohols, affording arylated aldehydes and ketones with a regioselectivity α/*β* depending on the steric hindrance around the double bond. Only trace amounts of the arylated allyl alcohols were obtained with that catalytic system.

Following on from this previous work, we decided to study deeply factors affecting the selectivity of these reactions. Preliminary experiments showed that Pd(OAc)$_2$ could be used as catalyst in place of the Pd−carbene complex, as the former provided, in TBAB, a similar product distribution. Reaction conditions were optimized to process 1 mmol of alkenol in 1 g of IL with 1.2 mol % of catalyst, performing the process by heating the catalyst source in the molten IL in the presence of reagents, so that Pd−nanocolloids were formed. Reaction times were carefully regulated to avoid the formation of byproducts coming from both the bis-arylation and the aldol condensation processes. Since it was reported[5] that a slight difference in the strength of bases used can have a striking effect on the regioselectivity, we started investigations evaluating a possible base effect on this process. Inspections were started on a monosubstituted olefin such as 1-octen-3-ol, using iodo- and bromo-benzene as arylating agents (Table 1).

As expected from a monosubstituted olefin, because of steric reasons, reactions were regioselective with respect to the addition of the aromatic group, affording predominantly to the *β*-substituted products **1a** and **1c**. Quite surprising, instead, was the influence of bases on both the catalyst activity and the isomerization process. Indeed, in TBAB as solvent, almost all the bases used, of both organic and inorganic nature, behaved similarly leading to a mixture of the sole arylated carbonyl compounds where the *β*-substituted product **1c** clearly prevailed (Table 1, runs 1−8). Under these conditions, reaction temperatures could not be lowered below 110 and 130 °C for iodobenzene and bromobenzene, respectively. Moreover, among the bases used, Bu_3N and NaOAc were the less efficient (Table 1, runs 7−8).

On the contrary, with TBAA as base, bromobenzene was rapidly reacted (0.7 h) at 90 °C and selectivity markedly changed affording an almost equimolecular mixture of the allyl alcohols

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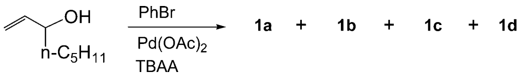
TABLE 2. Solvent Effect in the Heck Arylation of 1-Octen-3-ol Catalyzed by Pd(OAc)$_2$[a]



run	solvent	T [°C]	convn[b] (%)	t (h)	ratio (%)[b] **1a**/**1b**/ **1c**/**1d**
1[c]	TBAA	70	>99	0.5	90/6/4/0
2	DMAc	90	98	2	51/7/15/0[d]
3	DMF	90	94	2	72/8/15/0[e]
4	toluene	90	89	2	60/12/13/0[f]
5	NMP	90	81	6	58/5/28/0[g]
6	[bmim][BF$_4$][h]	90			
7	[bupy][BF$_4$][i]	90			

[a] General reaction conditions: solvent (1 mL), halobenzene (1.2 mmol), allyl alcohol (1 mmol), Pd(OAc)$_2$ (1.2 mol %); TBAA (2 mmol) stirred at 90 °C under inert atmosphere. [b] Conversions and product ratios evaluated by ^{1}H NMR. [c] For comparison, run 14 of Table 1 has been inserted. [d] 27% of **1a′** was formed. [e] 5% of **1a′** was formed. [f] 15% of **1a′** was formed. [g] 9% of **1a′** was formed. [h] [bmim][BF$_4$] = 1-butyl-3-methyl imidazolium tetrafluoroborate. [i] [bupy][BF$_4$] = *N*-butyl pyridinium tetrafluoroborate.

1a and **b** (overall yield 57%) and the carbonyl compound **1c** (43%, Table 1, run 9).

To verify the dependence of selectivity on the concentration of that base, we gradually increased the TBAA/TBAB ratio, observing thus a corresponding enhancement of the selectivity in favor of the allyl alcohols **1a** and **b** (Table 1, runs 9−11).

Subsequently, we replaced completely TBAB with TBAA by using this latter as both base and reaction medium. Under these conditions, we observed a twofold effect: (1) an extraordinary increase of the catalyst activity and (2) an almost complete inversion of selectivity in favor of the arylated allyl alcohols **1a** and **b** (Table 1, runs 12−20).

The first effect was evidenced by the request of much more milder reaction conditions; indeed, bromobenzene was reacted at 60 °C (Table 1, run 15) and iodobenzene was activated even at room temperature, although with minor selectivity (Table 1, run 20). As a consequence of the second effect, the amount of the carbonyl product **1c** was reduced to a percentage lower than 5% (Table 1, runs 14 and 18). Moreover, reactions carried out in TBAA were highly stereoselective, being the conjugated aromatic alcohol **1a** formed all times in high stereoisomeric ratio (*E*/*Z* ratio = ca. 98:2).

For comparison, the same reaction experiments carried out by using TBAA as base were executed in the common organic solvents. Results given in Table 2 showed that reactions carried out in molecular solvents were slower and occurred with both minor conversions and selectivity. In addition, they required higher reaction temperatures (not lower than 90 °C) and furnished variable amounts of the byproduct (*E*)-1-phenyloct-1-en-3-one (**1a′**) coming from the oxidation of **1a** (Table 2, runs 1−5). At the same time, also the other two different classes of ILs were tested (viz., an imidazolium and a pyridinium-based IL), but in both cases reactions did not occur at all (Table 2, runs 6−7).

To gain further insights on the TBAA effect, we extended investigations to other monosubstituted allyl alcohols by varying the substituents on both the substrate and the aromatic ring of the aryl halide. Table 3 summarizes the results clearly showing how the two catalytic systems **A** and **B**, on the basis of the two different ILs TBAB and TBAA, display an opposite selectivity affording predominantly the arylated carbonyl compounds and the conjugated allyl alcohols, respectively.

Undoubtedly, as it is often postulated in the literature,[4,8,13,14] the coordination effect exerted by the hydroxyl group is a key factor in explaining the high catalyst activity and selectivity in the Heck arylation of allyl alcohols. However, to elucidate the extraordinary IL effect observed in our reactions, also the following factors must be taken into account: (1) the large quantity of acetate anions in the reaction medium, (2) their weak ligand nature which may lead to the switching from the neutral to cationic mechanism, and (3) their enhanced basicity in the tetraalkylammonium ionic liquid.

On the basis of these assumptions, our results can be reasonably explained with the reaction mechanism depicted in Scheme 2. After the oxidative addition, the Ar−Pd−X species can undergo the two reaction pathways a and b depending on the nature of the ligand (X) bonded to palladium. When TBAB is used as solvent, and a conventional base such as NaHCO$_3$ is employed (catalytic method A), ligand X will be Br$^-$ or I$^-$ (path a).

Under these conditions, the coordination sphere of palladium would probably be filled by halide ions so that coordination of the starting alkenol, which affords the π-complex **C**, would be decelerated by the slow deligation of one of these ligands.[15] This could be the reason for the higher reaction temperatures required by the catalytic method A (110 ÷ 130 °C).

Then, for steric reasons, the migratory insertion of the aryl group occurs predominantly to the β-position of the alkenol giving the σ-complex **D**, while the addition of the aryl moiety to the α-position occurs to a minor extent (complex **E**). As the syn β-elimination can take place on both the sides of the carbon bonded to the metal, a mixture of arylated allyl alcohols and arylated carbonyl compounds is expected to be formed by action of the base. However, as in these cases where the Pd−H readdition−elimination mechanism can operate, the thermodynamically favored α/β-substituted carbonyl compounds are solely observed.

When TBAA is used as the reaction medium, halogen ion X$^-$ initially bonded to palladium is presumably replaced by acetate (path b), which readily dissociates facilitating the coordination of the starting alkenol and giving the cationic complex **F**. This could be the key factor explaining the high catalytic activity displayed by palladium in TBAA, which allows the metal to activate iodo- and bromoarenes at such low reaction temperatures (rt and 60 °C, respectively).

Migratory insertion on the double bond occurring on **F** can give the two σ-complexes **G** and **I**. In this case, the insertion of the aryl group to the β-position (complex **G**) is favored by steric reasons as well as by the formation of a chelate structure, which is reported[4,8,14] to be responsible for the high selectivity toward the conjugated allyl alcohol. Indeed, this form impedes the hydrogen atom (H$_c$) on the carbon bearing the hydroxyl group to reach the syn-relationship with palladium. As a consequence, the extraction of the benzylic hydrogen atom (H$_a$) should be the one and only pathway for the β-elimination. Finally, because acetate ion is more basic in TBAA,[16] it is

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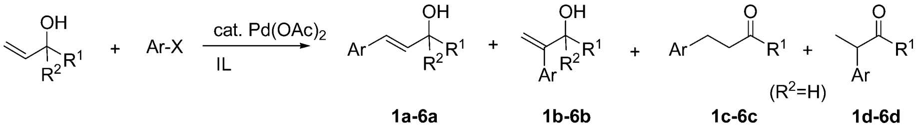
(15) As already reported by us (see refs 1d, 10−12), in the presence of TBAB or TBAA, the Ar−Pd−X species could be stabilized by interaction with the tetraalkylammonium salt affording more stable anionic complexes such as [ArPdX$_2$]$^-$ NR$_4^+$ or [ArPdX$_3$]$^{2-}$ 2NR$_4^+$ (where X = Br or AcO) depending on the free coordination sites on palladium. Indeed, if the reaction occurs on the nanoparticle surface, the number of coordination sites of Pd is smaller than four because of the linkage of the Pd atom to the metal bulk.

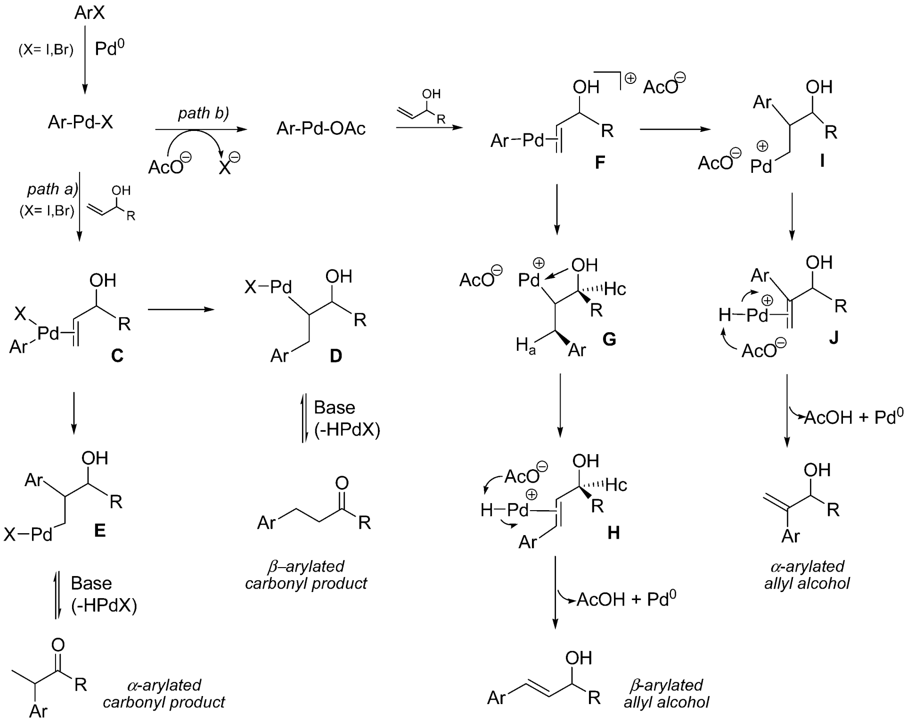
TABLE 3. Effect of the Substituents in Heck Arylation of Monosubstituted Allyl Alcohols[a]



run	R¹	R²	Ar	X	catalyst system[b]	*T* [°C]	*t* (h)	yields (%)[c]	product number	ratio[c] **a**/**b**/**c**/**d**
1	H	H	C_6H_5	Br	**A**	130	2	90	**2c**, **d**	0/0/85/15
2	H	H	C_6H_5	Br	**B**	70	0.5	87	**2a**, **b**	64/36/0/0
3	H	H	C_6H_5	I	**A**	110	1	90	**2c**, **d**	0/0/87/13
4	H	H	C_6H_5	I	**B**	50	0.5	84	**2a**, **b**	64/36/0/0
5	*n*-C_5H_{11}	H	C_6H_5	I	**B**	50	2.5	90	**1a**, **b**, **c**	80/11/9/0
6	CH_3	CH_3	C_6H_5	I	**B**	50	3	92	**3a**	100/0/0/0
7	*n*-C_5H_{11}	H	4-$CH_3C_6H_4$	Br	**A**	130	3	90	**4c**, **d**	0/0/94/6
8	*n*-C_5H_{11}	H	4-$CH_3C_6H_4$	Br	**B**	70	0.5	89	**4a**, **b**, **c**	86/6/8/0
9	*n*-C_5H_{11}	H	4-$CH_3OC_6H_4$	Br	**A**	130	4	85	**5c**, **d**	0/0/94/6
10	*n*-C_5H_{11}	H	4-$CH_3OC_6H_4$	Br	**B**	70	0.8	92	**5a**, **b**, **c**	82/9/9/0
11	*n*-C_5H_{11}	H	4-$CH_3COC_6H_4$	Br	**A**	130	1	87	**6c**, **d**	0/0/95/5
12	*n*-C_5H_{11}	H	4-$CH_3COC_6H_4$	Br	**B**	70	4	10[d]	**6a**, **b**, **c**	80/6/14/0
13	*n*-C_5H_{11}	H	4-$CH_3COC_6H_4$	Br	**B**	100	5	60	**6a**, **b**, **c**	80/5/15/0

[a] Reaction conditions: mixtures of aryl halides (1.5 mmol) and allyl alcohols (1 mmol) were stirred at the reaction temperature in the presence of the catalyst system (1.2 mol % of Pd) in molten TBAX (X = Br^- or AcO^-). [b] A: $Pd(OAc)_2$ (0.012 mmol) heated at 110 ÷ 130 °C in molten TBAB (1 g) until a dark suspension of Pd-nanocolloids is obtained; then, $NaHCO_3$ (2 mmol) and reagents (alkenol and ArX 1 and 1.2 mmol, respectively) are added. B: $Pd(OAc)_2$ (0.012 mmol), alkenol (1 mmol), and ArX (1.2 mmol) are added to TBAA (1 g) and the mixture is heated at the reaction temperature for the reaction times. [c] Evaluated by ^1H NMR. [d] Conversion 30%.

SCHEME 2. The Reaction Mechanism



presumable to expect a further accelerating effect by means of a rapid neutralization of the Pd−H species occurring intramolecularly on the π-complex **H**.[11]

As in this case where the Pd−H readdition−elimination mechanism can be completely ruled out, the formation of small amounts of carbonyl product in the reactions carried out in TBAA can be explained by admitting that the two reaction pathways a and b can operate simultaneously. The greater the contribution of truly cationic form of palladium complex intermediate (path b) is, that is, the poorer the coordination ability of ligand X, the higher the relative yield of allyl alcohol is.

A direct evidence of this hypothesis can be found comparing selectivity in the reactions carried out in the presence of variable TBAB/TBAA ratios (Table 1, runs 9−12). The greater the amount of TBAB in the reaction medium is, that is, the higher the presence of a good ligand for Pd such as Br^-, the higher the proportion of carbonyl products is and vice versa. Also, the selectivity in favor of the carbonyl products observed by using

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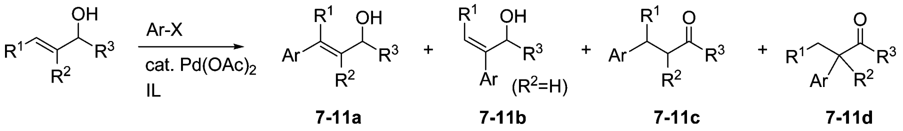
(16) Because of the tetrahedral structure of the tetraalkylammonium cation of TBAA, the positive charge on the nitrogen atom was shielded by the bulky butyl chains, and as a consequence, the more naked acetate anions proved to be more basic than in water.

TABLE 4. Heck Arylation of Disubstituted Allyl Alcohols Catalyzed by $Pd(OAc)_2$[a]



run	R^1	R^2	R^3	Ar	X	catalytic system[b]	T [°C]	t (h)	yields (%)[c]	product number	ratio[c] **a**/**b**/**c**/**d**
1	C_6H_5	H	H	C_6H_5	Br	**A**	130	6	90	**7b**, **c**, **d**	0/3/47/50
2	C_6H_5	H	H	C_6H_5	Br	**B**	80	0.5	92	**7a**, **b**	7/93/0/0
3	C_6H_5	H	H	C_6H_5	I	**A**	110	5	89	**7b**, **c**, **d**	0/5/46/49
4	C_6H_5	H	H	C_6H_5	I	**B**	80	0.5	87	**7a, b**	4/96/0/0
5	C_6H_5	H	H	4-$CH_3COC_6H_4$	Br	**A**	130	1	90	**8c**, **d**	0/0/40/60
6	C_6H_5	H	H	4-$CH_3COC_6H_4$	Br	**B**	100	6	20[d]	**8a**, **b**	10/90/0/0
7	C_6H_5	H	H	4-$CH_3OC_6H_4$	Br	**A**	130	6	78	**9b**, **c**, **d**	0/5/45/50
8	C_6H_5	H	H	4-$CH_3OC_6H_4$	Br	**B**	80	1.5	87	**9a**, **b**	6/94/0/0
9	H	CH_3	H	C_6H_5	Br	**A**	130	1	90	**10c**, **d**	0/0//95/5
10	H	CH_3	H	C_6H_5	Br	**B**	70	0.5	88	**10a**, **c**	43/0/21/0[e]
11	CH_3	H	H	C_6H_5	Br	**A**	130	2	90	**11c**, **d**	0/0/69/31
12	CH_3	H	H	C_6H_5	Br	**B**	80	8	85	**11a**, **b**	54/26/0/0[f]

[a] Reaction conditions: the same as Table 3. [b] A: $Pd(OAc)_2$ (0.012 mmol) heated at 110 ÷ 130 °C in molten TBAB (1 g) until a dark suspension of Pd-nanocolloids is obtained; then, $NaHCO_3$ (2 mmol) and reagents (alkenol and ArX 1 and 1.2 mmol, respectively) are added. B: $Pd(OAc)_2$ (0.012 mmol), alkenol (1 mmol), and ArX (1.2 mmol) are added to TBAA (1 g) and the mixture is heated at the reaction temperature for the reaction times. [c] Evaluated by ^1H NMR. [d] Conversion 25%. [e] 36% of the byproduct **10a′** was formed. [f] 20% of the byproduct **11b′** was formed.

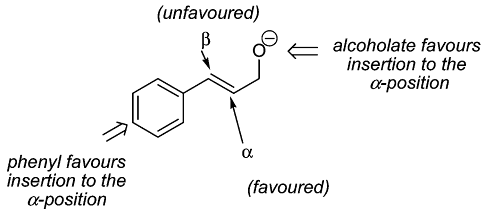
sodium acetate (Table 1, run 8) is explainable with these assumptions because of the low solubility of this base in TBAB. Most of the experimental evidence reported in this paper support the mechanism depicted in Scheme 2:

(1) The addition of the aryl moiety to the α-position (complexes **I** and **J**) occurs to a major extent in TBAA (ranging from 3% to 36%, see Tables 1−2) than in TBAB, where the α-product is obtained at a maximum of 6%. This strongly confirms that in TBAA the cationic mechanism operating as the coordination of the alkenol by the cationic complex should cause the polarization of the π system, resulting in a more directed migration of the aryl residue to the slightly more electrophilic α-position.[17]

(2) The variable amounts of the α-arylated allyl alcohols obtained in TBAA seem to be predictable on the basis of the structure of the starting alkenol. As can be seen in Table 3, the percentages of the α-arylated alcohols gradually decrease starting from 36%, in the case of the allyl alcohol (Table 3, run 4), to 11% for 1-octen-3-ol (Table 3, run 5), until 0% for 3-methyl-1-buten-3-ol (Table 3, run 6). This is in agreement with the acidity scale of the starting allyl alcohols (primary > secondary > tertiary) and falls in line with the hypothesis that the starting alkenol can be partially deprotonated by acetate, affording the corresponding alcoholate anion which, by enhancing the electron-rich character of the double bond, would favor addition to the α-position.

(3) Results in Table 3 show also that in TBAA as reaction medium, both neutral and electron-rich aryl halides proved to be more active than the corresponding electron-poor substrates. In fact, under the same conditions, bromobenzene (Table 1, run 14), *p*-bromotoluene (Table 3, run 8), and *p*-bromoanisole (Table 3, run 10) are completely converted in less than 1 h, while *p*-bromoacetophenone required higher reaction temperatures and longer reaction times (Table 3, runs 12−13). This is in contrast with the outcome of the analogous reactions carried out in TBAB (Table 1, run 1 and Table 3, runs 7, 9, 11) and the typical scale reactivity of aryl halides in the Heck reactions (electron poor > neutral > electron rich), but it is in complete agreement with a cationic mechanism.[17]

SCHEME 3. Directive Effects of Substituents on the Double Bond of Cinnamic Alcohol



(4) Further evidence supporting our hypothesis arises from the outcome of the Heck arylation of disubstituted alcohols (Table 4). Noteworthy is the high α-selectivity of the reaction in TBAA on the cinnamic alcohol with respect to the analogous process in TBAB (Table 4, runs 1−8). Indeed, because of its nature of primary alcohol, a sensible amount of alcoholate anion is expected to be formed by the action of the base. It appears evident in this case that directive effects of both the phenyl group and the alcoholate moiety add together to favor almost exclusively the formation of the α-allyl alcohol (Scheme 3).

The opposite trend of the selectivity toward either the arylated allyl alcohols (method B) or the carbonyl compounds (method A) was confirmed also with disubstituted olefins (Table 4). Results also confirm the opposite influence on the catalyst activity displayed by substituents on the aryl halides in the two catalytic systems. Indeed, an electron-poor aryl halide such as *p*-bromoacetophenone behaved as an activated aryl agent with method A and as a deactivated one with method B (Table 4, runs 5−6). Of course, an electron-rich aryl halide such as *p*-bromoanisole behaved in the opposite manner (Table 4, runs 7−8).

Excluding cinnamic alcohol, with disubstituted olefins bearing an alkyl chain on the double bond, the selectivity is complicated by the formation of arylated products coming from the

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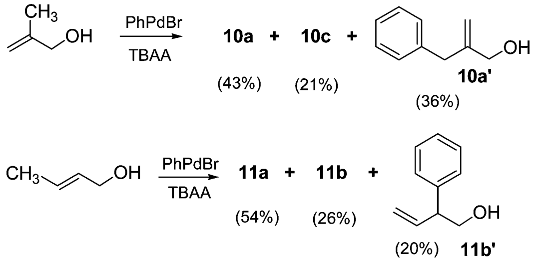
(17) The formation of a cationic complex intermediate is usually invoked by many authors to explain the enhancement of α-regioselectivity observed in the Heck arylation of unsymmetrical olefins, especially the electron-rich one. The cationic complex can be generated either by means of the assistance of halide scavengers (thallium(I) or silver(I) salts) or by spontaneous dissociation of good leaving groups such as the triflate. See, for example: de Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379−2411. Mo, J.; Xu, L.; Xiao, J. *J. Am. Chem. Soc.* **2005**, *127*, 751−760.

SCHEME 4. Selectivity Displayed by 1,1- and 1,2-Disubstituted Alkenols in TBAA



β-elimination occurring on the side of the alkyl chain. Two model examples are shown in Table 4: (1) the Heck phenylation of 2-methylprop-2-en-1-ol, a 1,1-disubstituted olefin, that in TBAA furnished, besides the expected β-arylated products **10a** and **10c**, also the terminal alkenol **10a′** (Scheme 4 and Table 4, run 10) and (2) the arylation of crotyl alcohol, a 1,2-disubstituted olefin, that afforded in TBAA the expected α- and β-substituted allyl alcohols **11a** and **11b** together with the byproduct **11b′** (Table 4, run 12). The same reactions carried out with method A occurred without side products (Table 4, runs 9 and 11).

Conclusions

In summary, our results proved to be of particular interest for the following reasons:

(1) The outcome of the arylation of allyl alcohols can be highly controlled by the catalytic systems A and B which are both highly selective. Aryl-substituted carbonyl compounds and the corresponding α,β-unsatured alcohols can be obtained by simply choosing the appropriate reaction medium and the base (TBAB/$NaHCO_3$ or TBAA, respectively). To our knowledge, this is the first case in the literature in which a so high selectivity can be reached on such substrates without using phosphane ligands, special arylating agents (e.g., triflates), and toxic or expensive additives (thallium and silver salts).

(2) Protocols A and B proved to be very simple and useful and do not require special care such as the inert atmosphere or particular manipulations; both reagents and catalyst source are mixed together in the IL, assuring this latter the almost immediate formation of the catalytically active species. In addition, the nature of surfactant of the tetraalkylammonium IL allows the stabilization of the Pd nanoparticles that constitute a reservoir of catalyst. This could be also the reason for which [bmim]- and [bupy]-based ILs are poor reaction media (Table 2, runs 6−7).[1d,10,11] However, in the case of reactions in TBAA (method B) at low temperatures, the formation of nanocolloids as catalyst reservoir has not been ascertained, and works are in progress to evaluate also the catalyst recycling.

(3) Finally, by using TBAA as the IL (method B), a very active Pd−cationic complex operates allowing the reactions to occur at so mild conditions to activate bromoarenes and iodoarenes at 60 °C and room temperature, respectively. This also constitutes, to our knowledge, an unprecedented result in the Heck couplings under phosphane-free conditions.

Experimental Section

General Procedure for the Heck Arylation of Allyl Alcohols in Molten Tetraalkyammonium Salt (Catalyst Systems A and B). In a 25-mL round-bottom flask, equipped with a magnetic bar, tetraalkylammonium salt (TBAB or TBAA) (1 g), $Pd(OAc)_2$, (2.7 mg, 0.012 mmol), alkenol (1 mmol), base (only in method A, 2 mmol), and aryl halide (1.2 mmol) were placed. In the case of using molecular solvents, a three-necked flask connected with a nitrogen line was used to create the inert atmosphere. For reactions carried out at room temperature (method B), TBAA (1 g), $Pd(OAc)_2$, and iodobenzene were added together and the mixture was melted at ca. 70 °C. Then, under vigorous stirring, the mixture was cooled at room temperature and the allyl alcohol was added.

All the reaction mixtures were heated under stirring at the reaction temperature and were monitored by glc (gas liquid chromatography) for a maximum of 8 h. Then, after cooling to room temperature, reaction mixture was washed with diluite HCl to remove most of both the tetraalkyammonium salt and the trialkylammine deriving from the IL decomposition. After the solvent removal, in vacuo, the reaction mixture was examined via ^1H NMR to evaluate the product ratio (see Supporting Information). Next, the whole reaction mixture was poured on a short pad of silica gel to get the overall yields reported in tables **1**−**3** and **4**.

Acknowledgment. This work was in part financially supported by Ministero dell'Università e della Ricerca Scientifica e Tecnologica, Rome, and the University of Bari (National Project: "Stereoselezione in Sintesi Organica: "Metodologie ed Applicazioni").

Supporting Information Available: General methods, experimental details, characterization data of the unknown compounds, and NMR spectra of reaction mixtures. This material is available free of charge via the Internet at http://pubs.acs.org.

JO070005F