Selective Palladium(II)-Catalyzed Dimerization of Styrenes and Acrylates in Molten Tetrabutylammonium Acetate as an Ionic Liquid

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Abstract: A method for the selective dimerization of styrenes and acrylates has been developed. The reaction is catalyzed by a very low amount of palladium acetate in molten tetrabutylammonium acetate without the need for any additional ligand. The use of this method enabled the coupling of substituted vinyl arenes in reasonable yields to give exclusively the (E,E)-1,4-diarylbutadiene motif within 7-10 h. Acrylates, on the other hand, exhibit higher reactivity, and the use of dibutyl acrylate resulted in the quantitative synthesis of dibutyl 2-methyleneglutarate in less than 2 h. This selectivity is unprecedented in the literature. The role of the ionic liquid and the different catalytic pathways involved in the two processes were also elucidated.

Introduction

The motif of 1,3-butadiene is commonly present in a variety of natural products and drug candidates that exhibit significant biological activity[1]. Additionally, dienes are a crucial focus for synthetic chemists since they offer numerous possibilities for functional group transformations, including a diverse range of C-C bond-forming reactions[2,3]. Given their importance, the synthesis of 1,3-dienes by coupling two vinyl fragments has attracted the attention of many research groups from the 1960s[4–6] to the present[1,3,7–9].

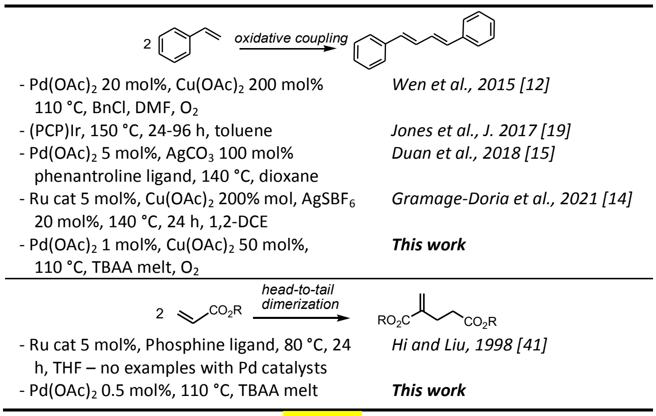
As an example, the oxidative dimerization of styrene to 1,4-diphenyl-1,3-butadiene (also called oxidative coupling, OCS) promoted by palladium acetate is a well-known method in organic synthesis[4,6,10], widely studied due to the importance of the diaryl conjugated dienes in the field of material science[11,12].

Several olefins substituted at the double bond like 1-methylstyrene, 1-1-diphenylethylene, vinyl acetate, etc., undergo this reaction. The double bond exclusively couples head-to-head, involving the least substituted carbon atom of the double bond, and during the reaction, Pd(II) is reduced to Pd(0), unless measures are taken to prevent the reduction. To this end, an oxidant is to be used, so the process can be pseudo-catalytic towards palladium(II)[13].

The oxidation or acetoxylation of the olefin, as well as its non-oxidative dimerization, are competitive processes, and in the presence of arenes, the olefin can be also arylated. Reactions are usually carried out in a polar solvent such as water or acetic acid, but also classic organic solvents and both homogeneous and heterogeneous palladium catalysts (recently also other metals) are known[1–3,7,8,12,14,15].

First examples of reactions were carried out with stoichiometric amounts of palladium and date back to the early ‘60s[4–6]. Next, from a mechanistic perspective, the process generated much interest[16]. Several kinetic studies were conducted, and many efforts have been made to make the method purely catalytic[17]. For this purpose, copper(II)[18] or silver(I) salts[15], and molecular oxygen[10], have been investigated as palladium oxidant agents.

In 2008, Loh et al. succeeded in the direct cross-coupling of 1,1-disubstituted alkenes with acrylates, catalyzed by 20% (mol%) of palladium acetate and one equivalent of copper acetate as the oxidant. A mixture of DMSO/acetic acid was used as the solvent, and it took 24 h to achieve good conversions at 80 °C[18].



- $Pd(OAc)_2$ 20 mol%, $Cu(OAc)_2$ 200 mol% 110 °C, BnCl, DMF, O_2	*Wen et al., 2015 [12]*
- (PCP)Ir, 150 °C, 24-96 h, toluene	*Jones et al., J. 2017 [19]*
- $Pd(OAc)_2$ 5 mol%, $AgCO_3$ 100 mol% phenantroline ligand, 140 °C, dioxane	*Duan et al., 2018 [15]*
- Ru cat 5 mol%, $Cu(OAc)_2$ 200% mol, $AgSBF_6$ 20 mol%, 140 °C, 24 h, 1,2-DCE	*Gramage-Doria et al., 2021 [14]*
- $Pd(OAc)_2$ 1 mol%, $Cu(OAc)_2$ 50 mol%, 110 °C, TBAA melt, O_2	***This work***
- Ru cat 5 mol%, Phosphine ligand, 80 °C, 24 h, THF – no examples with Pd catalysts	*Hi and Liu, 1998 [41]*
- $Pd(OAc)_2$ 0.5 mol%, 110 °C, TBAA melt	***This work***

Figure 1. Comparison with metal catalyzed reactions in the literature.

A few more protocols have been published in the past decade, and iridium[19] or ruthenium-based catalysts[14,20] have been reported, instead of palladium. As an example, an Iridium-Pincer complex was found to catalyze the dehydrogenative coupling of inactivated C-H bonds of substituted styrenes at 150 °C in toluene[19]. More recently, some authors have reported ruthenium-catalyzed oxidative homocoupling of acrylates and styrenes in good yields. Unfortunately, the reaction conditions were very harsh, as 140°C and 24 h were required to complete the reaction in 1,2-DCE as the solvent.

Furthermore, stoichiometric amounts of a silver salt and copper acetate were also required[14]. (Fig. 1).

Recently, Lin and coworkers, published an elegant highly stereoselective protocol for the synthesis of disubstituted and trisubstituted 1,3-dienes, based on a 1,4-palladium migration/Heck sequence.[21,22]

Because of the data reported above, it is clear that more environmentally compatible reaction conditions need to be investigated, starting with the solvent. In the last two decades, we have shown that a number of palladium-catalyzed reactions, such as carbonylation, Heck, Suzuki, Stille, and Ullmann couplings, can be performed with excellent yields and mild conditions by using Pd catalysts and tetrabutylammonium-based ionic liquids (ILs) as the reaction media[23–25]

Recently, some of us proposed a simple and high throughput Pd-catalyzed oxidative coupling between benzoic acids and vinylarenes or acrylates to furnish isocoumarins and phthalides *via* a selective C−H bond activation, in molten tetrabutylammonium acetate as the solvent and with very low percentage of ligand-free palladium acetate as the catalyst. Sub-stoichiometric amount of copper acetate was also required as the re-oxidant for the palladium[24]. Despite these neoteric media are increasingly proposed as ideal substitutes for traditional solvents in catalysis, especially in the field of C-C couplings[26–29], the use of ILs in this process has been totally neglected.

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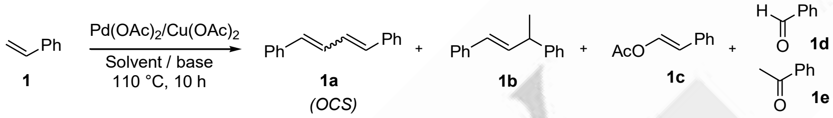
Table 1. Solvent scope in the oxidative coupling of styrene **1** (OCS) catalyzed by $Pd(OAc)_2$.[a]



Run	Solvent	Base	Convn. [%][b]	Products ratio [%]			
				1a	**1b**	**1c**	**1d-e**
1	acetic acid	-	35	95	-	<5	<5
2	pivalic acid	-	18	95	-	-	<5
3	H_2O	TBAOH	0	-	-	-	-
4	DMA	NaOAc	10	100	-	-	-
5	DMA	TBAA	18	100	-	-	-
6	DMSO	NaOAc	<5	100	-	-	-
7	toluene	NaOAc	<5	100	-	-	-
8	BMIM AcO	-	0	-	-	-	-
9	BuPy PF_6	-	95	-	Olig.	-	-
10	BMIM Cl	NaOAc	0	-	-	-	-
11	BMIM Br	NaOAc	8	100	-	-	-
12	BuPy Br	NaOAc	0	-	-	-	-
13	BuPy Cl	NaOAc	0	-	-	-	-
14	BuPy PF_6	NaOAc	95	-	Olig.	-	-
15	BuPy PF_6	TBAA	20	100	-	-	-
16	TBA CH_3SO_3	-	48	20			18
17	TBAA	-	98	53[c]	Olig.	-	<5
18	TBABr		47	10	Olig.		<5
19	TBACl		10	5	Olig.		<5
20	TBAA	TBAB	67	27	Olig.		<5
21	TBAA	TBA CH_3SO_3	75				<5

[a] Reaction conditions: In a 10 mL gastight vial a mixture of styrene (2.5 mmol), $Cu(OAc)_2$ (1.25 mmol), base (1.25 mmol), $Pd(OAc)_2$ (5,6 mg, 0.025 mmol, 1,0 mol%) in 0.5 ml of solvent (or 0.5g of ionic liquid) is heated under O_2 at 110 °C for 10 h. [b] Conversion was evaluated by GC-MS and by using stilbene as an internal standard. [c] Isolated yield.

Following our studies on this topic, we are now interested in examining the application of our conditions to the oxidative dimerization of styrene exploiting the activating effect exerted by the ionic liquid toward the Pd catalyst.

Herein, we present the first example of oxidative coupling of substituted vinyl-arenes to yield *(E,E)*-1,4-diaryl-1,3-butadienes promoted by Pd acetate in molten tetrabutylammonium acetate (TBAA) as the reaction medium. The analogous coupling of alkyl acrylates is also proposed.

Results and Discussion

Preliminary, styrene was used as the model substrate to optimize the Pd-catalyzed oxidative dimerization conditions (Table 1). With this method, nonoxidative dimerization, acetoxylation, oxidation to benzaldehyde or acetophenone, and double bond halogenations (when halogenated oxidants are used) can occur as competitive processes[2].

Initially, a solvent scope was carried out exploring a variety of molecular solvents and the most used ionic liquids. In these preliminary experiments copper acetate $Cu(OAc)_2$ was chosen as re-oxidant agent, based on previous results[24].

Coupling experiments were calibrated on 2.5 mmol scale of the olefin, 1 mol% of $Pd(OAc)_2$ and 1.25 mmol of copper acetate. Reaction temperature was initially set to 110 °C, to ensure the complete melting of all the ionic solvents under investigation and a balloon of O_2 was also used, to promote Pd re-oxidation.

The most plausible mechanism involves the σ-vinyl complex formation as the rate-determining step (eq. 1), followed by the rapid insertion of the olefin into the C-Pd bond and the β-elimination of palladium hydride (eq. 2-3).[2] Therefore, the presence of a base was thought to be essential to accomplish the reaction and, based on previous results[24], the acetate anion was chosen to this end.

$$PhCH{=}CH_2 + PdX_2 \xrightarrow{slow} PhCH{=}CHPdX + HX \quad (1)$$

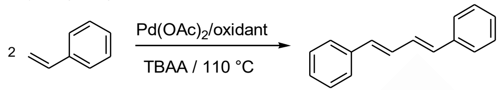
$$PhCH{=}CHPdX + PhCH{=}CH_2 \longrightarrow PhCH{=}CH\text{-}CH_2\text{-}CHPhPdX \quad (2)$$

$$PhCH{=}CH\text{-}CH_2\text{-}CHPhPdX \longrightarrow PhCH{=}CH\text{-}CH{=}CHPh + Pd^0 + HX \quad (3)$$

From data in Table 1 clearly emerged that common molecular solvents, e.g. acetic acid or DMA (Table 1, runs 1-7), as well as imidazolium- and pyridinium-based based ionic liquids (Table 1, runs 8-15) are unsuitable reaction media for these couplings, providing very low conversions and/or selectivities towards the diene product **1a**[2]. In contrast, according to our previous results[30,31], quaternary ammonium based ionic liquids proved to be more efficient in stabilizing palladium species giving higher conversions and selectivities (Table 1, runs 16-21). In particular, the most favorable outcome was achieved with tetrabutylammonium acetate (TBAA), reaching a quantitative conversion of the starting alkene, although the presence of oligomers lowered the isolated yield of the desired product **1a** to 53% (Table 1, run 17).

Notably, while BMIM-based ILs proved to almost inhibit the coupling totally (Table 1, runs 8,10-11), in the case of butylpyridinium hexafluorophosphate, styrene was completely converted into a mixture of not well characterized oligomers and such a disappointing result remained unchanged even upon adding a base such as NaOAc (Table 1, runs 9,14).

Table 2. Oxidant evaluation in the oxidative coupling of styrene **1** (OCS) catalyzed by $Pd(OAc)_2$. [a]



Run	Oxidant	Convn. [%]	Yield[%][b]
1	$CuSO_4$	7	38
2	$Cu(OAc)_2$	98	53
3	$Cu(CF_3SO_3)_2$	67	38
4	$CuBr_2$	23	55
5	Fe_2O_3	5 (7) [c]	100
6	$Fe_2(SO_4)_3$	6	100
7	Fe_3PO_4[d]	6	100
8	Ag_2CO_3	0	-
9	Riboflavin	0	-
10	1,4-Benzoquinone	0	-
11	t-BuOOH	58	0
12	H_2O_2	67	0
13	O_2	0	-

[a] Reaction conditions: In a 10 mL gastight vial a mixture of styrene (2.5 mmol), oxidant (1.25 mmol), base (1.25 mmol), $Pd(OAc)_2$ (5,6 mg, 0.025 mmol, 1,0 mol%) in 0.5 g of TBAA is heated at 110 °C for 10 h. [b] Yield was evaluated by GC-MS and by using stilbene as an internal standard. [c] In parenthesis, conversion at 24 h. [d] Dihydrated $Fe_3PO_4{\cdot}2H_2O$ was used.

However, when TBAA was used in combination with $BuPyPF_6$, the selectivity significantly changed in favor of the desired product **1a**, thus confirming the beneficial effect of the former IL, although the conversion remained low (Table 1, run 15).

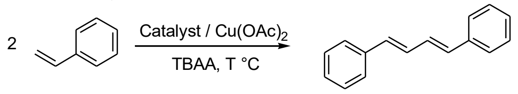
Next, performances of $Cu(OAc)_2$ were compared with those of other re-oxidants. From results listed in Table 2 emerged that copper(II) salts were found to be the most active (Table 2, runs 1-4). These findings are in line with the literature, where iron(III) and copper(II) salts are commonly employed as well as molecular oxygen[32,33]. However, when tested in ionic liquid, iron salts and molecular oxygen yielded poor results (Table 2, runs 5-7,13). Furthermore, silver carbonate and common organic oxidants failed (Table 2, runs 8-10), while the use of peroxides led to the formation of styrene oxide and by-products, as expected (Table 2, runs 11-12).

From these experiments also emerged that $Cu(OAc)_2$ must be used in 50% mol respect to the olefin, and all attempts aimed at reducing that quantity resulted in poor conversions and selectivities.

Next, attention was paid to further optimize reaction conditions in terms of catalyst source, loading, and reaction temperature.

As shown in Table 3, the best result was achieved using 1 mol% of Pd acetate at 110 °C (Table 3, run 2). In fact, although first-order kinetics with respect to the palladium(II) acetate are commonly assumed for this process[13], it was found that a catalyst concentration greater than 1 mol% afforded worser results (table 3, runs 3-4). This phenomenon is frequently observed in TBAA[24]. Similarly disappointing yields were observed with Pd amounts lower than 1% (Table 3, run 5).

Table 3. Optimization of reaction conditions in the oxidative dimerization of styrene to 1,4-diphenyl-1,3-butadiene in TBAA.[a]

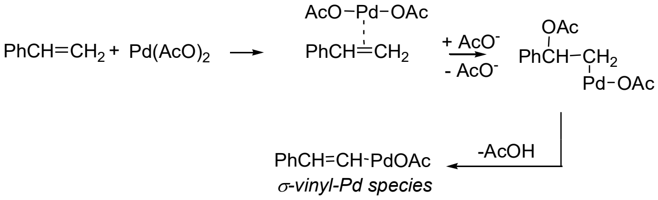


Run	Catalyst	Loading (mol%)	Temp. [°C]	Yield[%][b]
1	none	-	110	0
2	Pd(OAc)$_2$	1	110	53[c]
3	Pd(OAc)$_2$	3	110	38
4	Pd(OAc)$_2$	5	110	25
5	Pd(OAc)$_2$	0.5	110	41
6	Pd(OAc)$_2$	1	90	32
7	Pd(OAc)$_2$	1	130	36
8	PdCl$_2$	1	110	10
9	PdBr$_2$	1	110	15
10	Pd(DBA)$_2$	1	110	0
11	Rh$_2$(OAc)$_4$	1	110	8
12	RuCl$_3$	1	110	0
13	IrCl$_3$	1	110	<5

[a] Reaction conditions: In a 10 mL gastight vial a mixture of styrene (2.5 mmol), Cu(OAc)$_2$ (1.25 mmol), catalyst (see table) in 0.5 g of TBAA is heated under O$_2$ for 10 h. [b] Yield was evaluated by GC-MS and by using trans-stilbene as an internal standard. [c] Isolated yield.

Reactions were sensitive to the heating until 110 °C, after which a detrimental effect was observed probably due to the rapid thermally degradation of the quaternary ammonium salt TBAA (Table 3, runs 7). Likewise, at 90 °C, the reaction is still productive but lower yields were obtained (Table 3, run 6).

Regarding the palladium source, in agreement with the literature[3], palladium halides lead to modest conversions (Table 3, runs 8-9), as well as palladium in the zero-oxidation state (table 3, run 10). In this regard, it was observed that starting with Pd(0), the conversions in the first hour of the reaction are very low, suggesting the need for an induction time required for the oxidation of palladium before it can be catalytically active.



Scheme 1. Addition-elimination pathway leading to σ-vinylpalladium(II) species.

Presented results indicate that anions with coordinating ability towards palladium, such as halides, lead to relatively moderate conversion rates (see Table 3, runs 8-9). In contrast, anions that are poorly coordinating and possessing moderate basicity (such as acetate) have been found to offer good to excellent yields. Intermediate results have been observed with poorly coordinating and non-nucleophilic anions, such as PF$_6^-$ (Table 1, run 15).

Such results can somehow explain the crucial role played by acetate anion, whose presence as counterion in the Pd(II) source (Pd acetate), Cu(II) re-oxidant (Cu acetate), and in the ionic liquid medium (TBAA), seems to be mandatory.

Indeed, the formation of the vinylpalladium(II) species shown in eq. 1 is to be considered the rate determining step of the coupling. It is thought to occur by an electrophilic substitution of a vinyl hydrogen by Palladium through an addition-elimination process of acetate anion to the double bond, promoted by a preliminary π-coordination of Pd(II) according to scheme 1[34].

The addition plausibly occurs more rapidly with acetate anion, being this latter very abundant as counter ion of the solvent. In addition, its nucleophilicity is enhanced due to the shielding effect towards positive charge exerted by the bulky alkyl chains in tetraalkylammonium cations. The elimination mechanism belongs to the class of 1,2 eliminations in which the effect of the substituent is important.

The elimination is of a E2 type with a synchronous detachment and transfer of the proton to a base, which in this case is the solvent. The influence of the substituent can be mesomeric, inductive or steric. For instance, the presence of aryls to the α-position can enhance the formation of a σ-vinylpalladium(II) species by facilitating the elimination of acetic acid. Furthermore, the reaction can be accelerated by the rapid neutralization of acetic acid by the ionic liquid, which has an overall beneficial effect on the reaction.

With the optimized conditions in hand, a substrate scope was conducted to test applicability and limitations of the method.

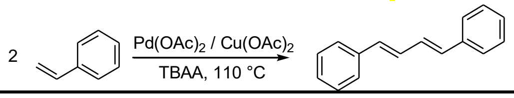
Results in Table 4 show a homogeneous range of yields for a series of substituted styrenes, with dimerization that appeared to be not affected by the nature of electron-withdrawing or electro-donating group of the substituents on aromatic ring. Noteworthy, alpha-methyl styrene, which is a 1,1-disubstituted olefin, was found to be almost unreactive (Table 4, product **7**).

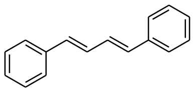
Similarly, other α,α disubstituted olefins like 1,1-diphenylethene or β-chloroolefins, vinyl ether and vinyl acetate proved to be inactive (data not shown). Also, vinyl naphthalene gave a very low yield (Table 4, product **9**) probably due to steric hindrance. In the case of divinylbenzene, the conversion of the substrate was complete, furnishing an insoluble compound (table 4, product **6**). The presence of two couplable sites on the same molecule suggests the formation of an insoluble oligomer, thus providing an alternative synthesis of highly conjugated oligo/polymers. Regarding stereochemical aspects, reaction resulted highly stereoselective, since only *(E,E)*-dienes were obtained, or with only very low amount of other isomers (< 5%), in some cases.

Encouraged by these satisfactory results, this methodology was extended to alkyl acrylates.

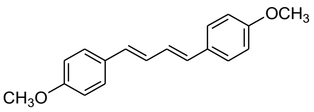
Disappointingly, the application of the previous protocol (Pd/Cu//TBAA) to these substrates failed in giving the expected head-to-tail dimerization product of acrylate, namely dibutyl 2-methylene glutarate (**DMG**) (Table 5, entry 1).

Table 4. Substrate scope and limitations of the reaction.[a]

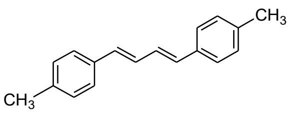




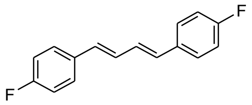
1a,7h, 53%



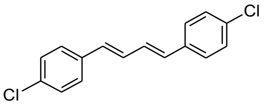
2, 8h, 48%



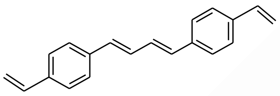
3, 8h, 41%



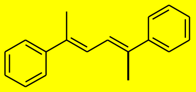
4, 8h, 33%



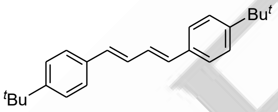
5, 8h, 41%



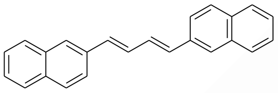
6, 12h, N.R.



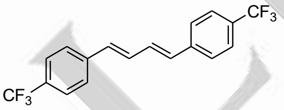
7,12h,11%



8, 8h, 41%



9, 12h, 8%



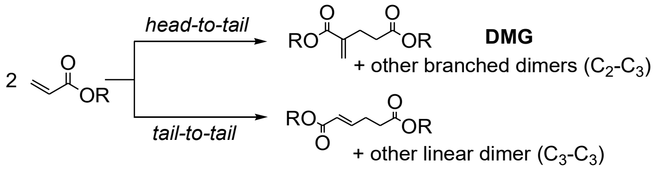
10, 8h, 47%

[a] Reaction conditions: In a 10 mL gastight vial a mixture of styrene (2.5 mmol), oxidant (1.25 mmol), $Pd(OAc)_2$ (5,6 mg, 0.25 mmol, 1 mol%) in 0.5 g of TBAA is heated under O_2 at 110 °C for the proper reaction time (h). Isolated yields.

Surprisingly, when the re-oxidant $Cu(AcO)_2$ was removed, conversion into **DMG** was complete and highly selective in only 3 h (Table 5, entry 2).

Consequently, attention was paid to studying the dimerization reaction, which surprisingly seemed to occur very smoothly under these simple and relatively mild conditions (1 mol% of Pd acetate in TBAA at 110 °C).

In principle, this reaction can occur in a tail-to-tail (C_3-C_3) or a head-to-tail (C_2-C_3) manner, affording linear or branched dimers, respectively (scheme 2).[35]

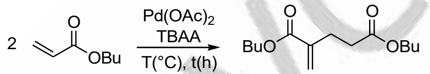


Scheme 2. Pathways for dimerization of acrylates.

Linear dimers are of paramount importance for preparing adipic acid, the precursor of nylon-6,6. and cyclopentenoic compounds[36].

Branched dimers such as dialkyl-2-methylenglutarate (**DMG**), dialkyl-2-methyl-2-pentendioate and dialkyl-4-methyl-2-pentendioate are often used as monomers in copolymerization reactions with styrene.

Table 5. Head-to-tail dimerization of butyl acrylate in TBAA.[a]



Entry	$Pd(OAc)_2$ (mol%)	T (°C)	t (h)	$Cu(OAc)_2$ [mol%]	Yields[b] [%]
1	1	110	7	50	<5%
2	1	110	3	-	100[d]
3	**0.5**	**110**	**2**	**-**	**100 (94)**[c]
4	0.5	90	3	-	73
5	0.5	120	3	-	37
6[e]	0.5	110	3	-	N.R.
7	-	110	2	-	7%

[a] Reaction conditions: butyl acrylate 2.5mmol, IL 0.5 g, $Pd(OAc)_2$ (2,8 mg, 0.5 mol%) in 0.5 g of TBAA, at 110 °C. [b] Yield based on GC-MS analysis with external standard. [c] Isolated yield. [d] Significant presence of isomers and trimer. [e] TBABr as ionic liquid solvent.

They can also be used in aldol-type condensations and other annulation reactions due to the presence of 1,5-bicarbonyl moiety[37,38].

Head to tail dimerization of acrylates, also known as Rauhut–Currier reaction, is known to be promoted by nucleophiles such as amines or bulky tertiary phosphines[39],[40,41]. However, reactions catalyzed by metals are very limited. Among these latter, ruthenium[42] and iridium[43] have been used, whereas examples of selective reactions catalyzed by palladium are totally unexplored in the literature.

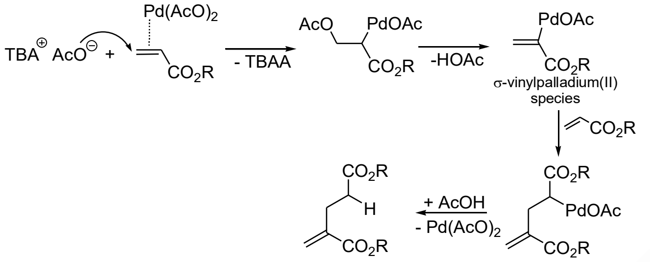
After the preliminary experiments, dimerization conditions were further optimized by varying catalyst loading, temperature, reaction time and ionic medium (Table 5, entries 3-6). From the screening emerged that Pd concentration could be lowered until 0.5%, as well as reaction time, that could be reduced to 3 h, while the optimal temperature and ionic medium were established to be 110 °C and TBAA, respectively (Table 5, entry 3).

Finally, the blank reaction conducted without $Pd(AcO)_2$, confirmed that Palladium is truly a catalyst for this reaction (Table 5, entry 7).

To the best of our knowledge, the high activity and selectivity displayed by Pd in giving the dimerization of acrylate in TBAA, has no precedents among the similar metal-catalyzed reactions reported in the literature, whether they are carried out in molecular solvents or in ionic liquids[39,42,43].

A plausible mechanism accounting for these experimental results is shown in scheme 3. It should start with the formation of σ-vinylpalladium(II) species with opposite regioselectivity respect to that reported in scheme 1, occurring by the nucleophilic addition of acetate of the ionic medium to the β-position of acrylate.

Then, the σ-vinylpalladium(II) species would give a migratory insertion to the double bond of another molecule of the substrate and subsequently the resulting σ-alkylpalladium(II) species should undergo to an electrophilic substitution with AcOH afforDing **DMG** and restoring Pd(OAc)$_2$ catalyst.



Scheme 3. Tentative explanation of head-to-tail dimerization mechanism.

Nevertheless, an alternative or parallel mechanism based onto a more classical nucleophilic catalysis exerted by acetate ions of the solvent and mediated by the presence of palladium (II) cannot be completely ruled out[39,42].

Conclusion

In conclusion, we presented here a new protocol for the dimerization of vinyl arenes and acrylates catalyzed by Pd(OAc)$_2$ and conducted in a tetraalkylammonium based ionic liquid (TBAA). In case of substituted styrenes, reaction proceeds via oxidative coupling through a double C$_{\text{vinyl}}$-H activation at 110 °C with palladium amounts 10-20 times lower than those of the analogous processes reported in the literature[12,14,15,19]. Also, the protocol does not require neither ligands nor expensive or toxic oxidants, such as silver salt, but only copper acetate. The stereochemical outcome is highly selective affording (*E,E*)-1,4-diaryl-1,3-butadiene derivatives, exclusively. Isolated yields range from 53% to 33%, in line with the literature.

An analogous protocol applied to acrylate resulted in a highly efficient and regioselective dimerization that has no precedents in the literature among the similar metal catalyzed processes. With only 0.5 mol% of palladium acetate, at 110 °C and in TBAA, the exclusive head-to-tail dimerization of butyl acrylate is complete in only 2 h affording dibutyl-2-methylenglutarate (**DMG**).

For both processes, the enhanced nucleophilic properties of acetate ion in the ionic medium, due to its poor solvation by shielded counter cations, appears to be crucial to promote the addition to the double bonds leading to vinylpalladium species. Studies are underway in order to gain more mechanistic evidence and to improve the yields in the homocoupling of vinylarenes.

Experimental section

General Remarks. Starting reagents (styrenes and butyl acrylate), oxidants (1,4-benzoquinone, Fe_2O_3, Fe_2SO_4, Fe_3PO_4, Ag_2CO_3, Riboflavin, t-BuOOH, H_2O_2), catalysts (Pd(OAc)$_2$, $PdCl_2$, $PdBr_2$, Pd(DBA)$_2$, $Rh_2(OAc)_4$, $RuCl_3$, $IrCl_3$) and NaOAc (≥99%, Merck), are commercially available and were used without further purification. Copper salts (sourced by by Aldrich or Fluka) were dried under vacuum overnight before their use. N,N-dimethylacetamide (DMA) and dimethylsulfoxide (DMSO), were dried and then distilled before the use. Ionic liquids 1-butyl-3-methylimidazolium bromide ([Bmim] Br, ≥98.5% Aldrich), 1-butyl-3-methylimidazolium acetate ([Bmim] OAc, ≥98%, ABCR), 1-butyl-3-methylimidazolium chloride ([Bmim] Cl, ≥99.0% Fluka), tetrabutylammonium bromide (TBABr, ≥99.0% Fluka), tetrabutylammonium acetate (TBAA, ≥99.0% Fluka), tetrabutylammonium chloride (TBACl, ≥99.0% Fluka) tetrabutylammonium methansulfonate (TBA CH_3SO_3, ≥97.0% Aldrich), 1-butylpyridinium esafluorophosphate (BuPyPF$_6$, ≥98%, Aldrich), 1-butylpyridinium bromide (BuPyBr, ≥99%, Aldrich), 1-butylpyridinium chloride (BuPyCl, ≥98%, Aldrich) are commercially available and were used without further purification. Tetrabutylammonium hydroxide dihydated $Bu_4NOH \times H_2O$ (40% in H_2O, Aldrich) was used as received.

General procedure for synthesis of (*1E,3E*)-1,4-diaryl-1,3-butadiene (1a-10). In a 10 mL vial having a side-arm connected to an oxygen line and equipped with a screw cap and a magnetic bar, 0.5 g of TBAA, 2.5 mmol of styrene, Pd(OAc)$_2$ (0.5 mol%), Cu(OAc)$_2$ (1.25 mmol) were added. The mixture was heated under stirring at 110 °C for the proper reaction times (depending on the substrate, generally 10 h). For the products identification preliminary GC-MS analyses were performed by treating weighed aliquots of reaction mixture with aqueous HCl and extracting with ethyl acetate. For evaluating conversions and yields of tables 1-2-3-4, reacted styrene and formed products were detected by GC-MS analyses by adding to the extracted aliquots proper amounts of trans-stilbene as an external standard. To evaluate yields of diaryl-butadienes (Table 4) and to ensure the identification of the main reaction products, the whole reaction mixture was washed with aqueous HCl and extracted with ethyl acetate. Then, the combined organic layers were dried over anhydrous $MgSO_4$, the solvent removed in vacuo and the crude mixture was chromatographed on silica gel (eluent hexane/ethyl acetate). The isolated products were identified by comparison of NMR and GC-MS spectra with those reported in the literature. All products are known.

General procedure for synthesis of dibutyl-2-methylenglutarate. In a 10 mL vial having a side-arm connected to an oxygen line and equipped with a screw cap and a magnetic bar, 0.5 g of TBAA, 2.5 mmol of butylacrylate, Pd(OAc)$_2$ (0.5 mol%) were added. The mixture was heated under stirring at 110 °C for the proper reaction times. For the products identification preliminary GC-MS analyses were performed by treating weighed aliquots of reaction mixture with aqueous HCl and extracting with ethyl acetate. For evaluating conversions and yields of dibutyl-2-methylenglutarate (table 5), reacted acrylate and formed products were detected with GC-MS analyses by adding to the extracted aliquots proper amounts of trans-stilbene as an external standard. To evaluate yields of dibutyl-2-methylenglutarate (table 5) and to assure the identification of the main reaction products, the whole reaction mixture was washed with aqueous HCl and extracted with ethyl acetate. Then, the combined organic layers were dried over anhydrous $MgSO_4$, the solvent removed in vacuo and the crude mixture was chromatographed on silica gel (eluent hexane/ethyl acetate 6:1) affording 300,7 mg (yield 94%) of dibutyl-2-methylenglutarate as oil.

Supporting Information

The authors have cited additional references within the Supporting Information.[43]

Keywords: acrylates • dialkyl methyleneglutarates • diaryl butadienes • ionic liquids • oxidative dimerization

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