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Ligand-free palladium-catalyzed tandem pathways for the synthesis of 4,4-diarylbutanones and 4,4-diaryl-3-butenones under microwave conditions

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National Science Centre (NCN, Poland), Grant/Award Number: 2014/15/B/ST5/ 02101 Two efficient Pd-catalyzed tandem pathways for the synthesis of 4,4-diaryl-2butanones and 4,4-diaryl-3-buten-2-ones were elaborated. The first step in both procedures was the Heck coupling of methyl vinyl ketone (MVK) and various aryl iodides leading to 4-aryl-3-buten-2-one with the yield of up to 92% in 1 hr. The second step performed with the same catalyst and a new portion of aryl iodide in the presence K_2CO_3 as a base produced 4,4-diaryl-3-buten-2-ones in high yield. Reaction selectivity changed completely to saturated 4,4-diaryl-2butanones, reductive Heck products, when a tertiary amine was used instead of K_2CO_3 . Due to the application of microwave irradiation (MW), the desired products were obtained in high yield in a short time (4 hr), using 0.5 mol% of the Pd (OAc)₂ catalyst without additional ligands.

KEYWORDS

diaryl-ketones, Heck coupling, MW irradiation, palladium, reductive Heck coupling

1 | INTRODUCTION

Mono- and diarylated ketones are a class of compounds with a wide potential of application. Especially important among them are chalcones^[1–7] and β -aryl- α , β -unsaturated enones; for example, 4-aryl-3-buten-2-ones.^[8-10] The high biological activity of many chalcone derivatives makes them important materials for the fabrication of drugs against cancer or atherosclerosis.^[1-4] They can also be used in the production of fluorescent probes^[5,6] or optical materials.^[7] Moreover, β-substituted carbonyl compounds are the backbone of active biomolecules, such as enokipodine B (fungal biomarker) or paroxetine (antidepressant).^[11] Synthetic methods used for the preparation of β -arylketones are usually based on a coupling between methyl vinyl ketone (MVK) and various aryl reagents in the presence of palladium catalysts.^[12-19] Further functionalization, leading to appropriate β -diarylketones, can be performed using synthetic tools that form a new carbon-carbon bond: the Heck reaction^[20-23] or the

reductive Heck reaction (conjugate addition).^[24–33] Both of those strongly related reactions,^[22,31,32] proceeding with the formation of the same alkyl-palladium-halide transition complex, have been the subject of intensive research for many years.^[24,25,27] The currently available data confirm that the Heck arylation is a much recognized method, especially due to the possibility of using various easily available aryl halides.^[22]

In contrast, in palladium-catalyzed reductive Heck arylation, mostly different organometallic compounds have been applied as the source of the aryl group. Grignard compounds,^[34,35] organoboron compounds,^[36,37] organozincs,^[38] organosilicons^[39–41] and other organometallic reagents have been used in the presence of copper, rhodium, or palladium catalysts. However, due to the high cost of these reagents, their low stability in reaction conditions or in the presence of water, replacing them with aryl halides is a favorable alternative. For the first time efficient palladium-catalyzed reductive Heck arylation with aryl halides was described in 1983 by Cacchi

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and co-workers.^[24] The method they developed involved the use of iodobenzene derivatives and corresponding enones or enals with the application of reducing agents such as NEt₃, Bu₄NI, or HCOOH.^[24] They observed that the nature of the base had a significant effect on the selectivity of the reaction and the type of product obtained. In the presence of inorganic bases like NaHCO3 or CH₃COONa, vinyl substitution occurred, while in the case of a tertiary amine, the reaction course changed towards a reductive Heck product.^[25] A similar result was obtained by Minnaard et al., who reported an efficient Pd-NHCcatalyzed Heck reaction and the conjugate addition of aryl iodides and β -substituted- α , β -unsaturated enones in the presence of CsOPiv and NBu₃, respectively.^[27] It is noteworthy that, in recent years, the progress of studies on conjugate addition has aided the search for different arylating agents, such as sodium arylsulfinates,^[42] arylsulfonyl hvdrazides^[43] or benzenesulfonyl chlorides.^[44] Nevertheless, the direct palladium-catalyzed reductive arylation of ketones with aryl halides has been scarcely reported.

The broad application of aryl ketones^[8–10] and their derivatives strongly motivates the development of selective and efficient synthetic methods leading to these compounds. In most cases reported in the literature, the arylation of aryl ketone to get β , β -diarylketone has been studied, while the synthesis of the first aryl ketone has not been discussed in this context. Our approach, presented in this paper, was based on a tandem process involving two arylation steps with the same catalyst, without the isolation of the first aryl ketone (Figure 1). The second modification consisted in the application of MW irradiation instead of conventional heating.^[12,45–47] It was expected that this would shorten the reaction time and save energy.

2 | EXPERIMENTAL

1. Arylation of 3-buten-2-one followed by a reductive Heck reaction

The reaction was carried out in a special microwave tube under microwave irradiation. The reagents, aryl iodide (1.34 mmol), NaHCO₃ (1.25 mmol; 0.1050 g), Pd (OAc)₂ (0.5 mol%, 0.001504 g), 3-buten-2-one (2.01 mmol; 0.163 cm³), and DMF/H₂O = 3/2 (2.5 cm³) were introduced to the microwave tube. Next, the tube with the reaction mixture was stirred under microwave conditions at 120 °C for the 1 hr. After that time, more aryl iodide (1.34 mmol) and tripropylamine (1.25 mmol; 0.236 cm³) were added and microwave heating continued for 3 hr at the same temperature. When the reaction time was finished, the organic products were separated by extraction with diethyl ether (10 cm³ and three times with 5 cm³). The products were GC–MS-analyzed (Hewlett Packard 8454 Å) with mesitylene (75 µl) as the internal standard.

2. Arylation of 3-buten-2-one followed by a Heck reaction

The reaction was carried out in a special microwave tube under MW irradiation. The reagents, aryl iodide (1.34 mmol), NaHCO₃ (1.25 mmol; 0.1050 g), Pd (OAc)₂ (0.5 mol%, 0.001504 g), 3-buten-2-one (2.01 mmol; 0.163 cm³), and DMF/H₂O = 3/2 (2.5 cm³) were introduced to the microwave tube. Next, the tube with the reaction mixture was stirred under microwave conditions at 120 °C for 1 hr. After that time, more aryl iodide (1.34 mmol) and K₂CO₃ (1.25 mmol; 0.1728 g) were added and MW heating continued for 2 hr at the same



temperature. After that time, the organic products were separated by extraction with diethyl ether (10 cm³ and three times with 5 cm³). The products were GC–MS-analyzed (Hewlett Packard 8454 Å) with mesitylene (75 μ l) as the internal standard.

3 | **RESULTS AND DISCUSSION**

3.1 | Heck arylation of methyl vinyl ketone (MVK)

The Heck arylation of 3-buten-2-one (MVK) by PhI was studied as the first reaction to obtain a substrate for further functionalization. Under the applied conditions, using MW, the formation of the desired product, 4-phe-nyl-3-buten-2-one **3R**, was quite efficient already in 1 hr; however, some amount of another product, diarylated ketone, **4RR**, was also observed (Figure 2). Thus, the optimization of the reaction parameters aimed at an increase of **3R** yield.

First, different palladium catalysts were tested (Figure 3), and Pd (OAc)₂ was found superior to the others, giving the highest yield of **3R**, 81%. Interestingly, palladium complexes without phosphorus ligands were more active than complexes bearing phosphito ligands. The oxidation state of palladium did not influence the reaction course, and similar results were obtained with Pd (II) (Pd (acac)₂, PdCl₂(CH₃CN)₂) and with Pd(0) (Pd₂(dba)₃) (Figure 3).

The screening of different bases enabled the selection of NaHCO₃ as the best one for the synthesis of **3R**, while other bases, such as carbonates, promoted the formation of diarylated ketone. For example, the application of K₂CO₃ or Cs₂CO₃ made it possible to produce symmetric 4,4-diphenyl-3-buten-2-one with yields of up to 30% (Figure 4).

Thus, optimized conditions for the efficient synthesis of **3R** were defined as 0.5 mol% of Pd $(OAc)_2$, NaHCO₃ as a base, 160 °C, and 1 h under MW. These conditions were applied to obtain the substrate **3R** for a tandem reaction, aimed at the synthesis of diarylated butanone containing two different aryl groups.



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FIGURE 3 Optimization of the palladium catalyst for the Heck arylation of 3-buten-2-one.Reaction conditions: 1.34 mmol 3-buten-2-one (MVK); 1.34 mmol PhI; 0.5 mol% Pd (OAc)2; 1.25 mmol NaHCO3; 1 hr; 160 °C; MW; 2.5 cm3 DMF, 0.5–3 bar



FIGURE 4 Optimization of the base for the Heck arylation of 3buten-2-one.Reaction conditions: 1.34 mmol 3-buten-2-one (MVK); 1.34 mmol PhI; 0.5 mol% Pd (OAc)2; 1.25 mmol base; 1 hr; 160 [°C]; MW; 2.5 cm3 DMF, 0.5–3 bar

3.2 | Tandem synthesis of 6RR'

A tandem experiment focused on the synthesis of **6RR'** was performed, in the first step applying optimized conditions for the synthesis of **3R**, which was obtained with a yield of 81% (Figure 5). Next, without the isolation of **3R**, another aryl iodide, p-iodoanisole, was introduced



FIGURE 2 Heck arylation of methyl vinyl ketone with phenyl iodides

R: H; OMe; Me



reaction

FIGURE 5 Tandem Heck reaction leading to 4-(4-methoxyphenyl)-4-phenyl-2-butanone

to the same vessel together with amine. Amine was chosen for this reaction because, according to the literature data, the presence of alkyl amine should facilitate reductive coupling and the formation of saturated diarylketone.^[24,25,27]

The results obtained with tripropylamine, tributylamine, and diisopropyl-ethylamine are presented in Table 1.

The yield of the desired product, 6RR' (R = H; R' = OMe), was similar for the three tested amines, amounting to 69-72%. The second product, unsaturated ketone, was formed with a yield of up to 27% as a mixture of E and Z isomers with the E/Z ratio of *ca*. 2. For comparison, reactions were performed at a lower temperature, 75 °C, using NEt₃ and NPr₃; however, only ca. 6% of 6RR' was formed in these conditions. Attempts to use other additives with potentially reducing activity instead of alkyl amines failed. In the presence of water, iPrOH, or CH₃COOH, only 4-12% of 4RR' was obtained, while 6RR' was not found (Table 2).

3.3 | Coupling reactions in the presence of water

The introduction of water to the reaction medium aimed at the improvement of both steps of the catalytic reaction, starting from the first coupling leading to 3R. That idea

TABLE 1 Heck synthesis of β , β -diaryl-2-butanones under MW conditions in the presence of different amines

Entry	Amine [mmol]	Conversion 3R [%]	6RR' [%]	4RR' (E/Z) [%]
1	NBu ₃	89	69	14/6
2	(<i>i</i> Pr) ₂ NEt	95	68	20/7
3	NPr ₃	88	72	11/5

Reaction conditions: Step I: 1.34 mmol 3-buten-2-one (MVK); 1.34 mmol PhI; 0.5 mol% Pd (OAc)2; 160 °C; 1 hr; MW; 0.5-3 bar

Step II: 1.34 mmol p-iodoanisole; 1.25 mmol amine, 120 °C; 1 hr; MW

TABLE 2 Testing of different additives in the reductive Heck

Entry	Reducing agent [mmol]	T[°C]	4RR' [%]
1 ^a	-	160	4
2	iPrOH (6.54)	75	6
3	iPrOH (32.70)	75	4
4	H ₂ O (27.78)	75	10
5	СН.СООН (1.25)	120	12

Reaction conditions: Step I: 1.34 mmol 3-buten-2-one (MVK); 1.34 mmol PhI; 0.5 mol% Pd (OAc)2; 160 °C; 1 hr; MW; 0.5-3 bar

Step II: 1.34 mmol p-iodoanisole; 120 °C; 1 hr; MW

^aResults obtained after the first step.

was based on our earlier studies on the arylation of allylic alcohols, where water improved the yield of the product.^[19] It was found that water increased the conversion of MVK to ca. 100%; however, selectivity to 3R decreased due to the formation of a diarylated ketone, 4RR $(\mathbf{R} = \mathbf{H})$, with a yield of 13–16% (SI, Table 2). The increase of the amount of water promoted a decrease in the yield of **3R** to 76% at the DMF/H₂O ratio of 3/2. Concerning the effect of the base, similar results were obtained for three bases, NaHCO₃, Na₂CO₃, and KHCO₃ at DMF/H₂O = 4/1 (SI, Table 2). Thus, the kind of base did not influence the reaction course.

The ratio of the substrates, [PhI]/[MVK], was the next parameter changed during the optimization of the reaction conditions. Figure 6 presents the dependence of the yield of 3R on the substrate ratio and the water amount.

With an increase in the amount of MVK, PhI conversion increased, and only the product 3R (R = H) was formed with the yield of 90% at [PhI]/[MVK] = 1/1.5 in DMF. In a DMF/H₂O mixture, the conversion of PhI reached 100%, and the yield of 3R was 95%.

Considering the ratio $DMF/H_2O = 3/2$ as the best one, different temperatures were tested (Figure 7).

It was found that the yield of **3R** was only slightly lower at 130 °C and 120 °C than at 160 °C, while only 74% of 3R was obtained at 110 °C (Figure 7). In all cases,



FIGURE 6 Influence of the PhI: MVK ratio and water on the yield of the productsReaction conditions: 1.34 mmol PhI; 0.5 mol% Pd (OAc)2; 1.25 mmol NaHCO3; 1 hr; 160 [°C]; MW; 2.5 cm3 DMF or DMF/H2O, 0.5–3 bar



FIGURE 7 Optimization of the Heck reaction temperature at PhI/MVK = 1/1.5Reaction conditions: 2.01 mmol 3-buten-2-one (MVK); 1.34 mmol PhI; 0.5 mol% Pd (OAc)2; 1.25 mmol NaHCO3; 1 hr; MW; 2.5 cm3 DMF/H2O (3/2), 0.5–3 bar

a small amount of biphenyl, up to 6%, was also formed. The reaction at 120 °C was also performed using conventional heating, and after 6 hr the yield of **3R** was 94%. The same result was obtained under MW already after 1 hr confirming the high efficiency of MW irradiation.

Conditions optimized for the synthesis of 3R in the DMF/H₂O medium under MW irradiation were also applied for other aryl iodides, p-iodoanisole and p-iodotoluene. Very good results were obtained, as shown in Figure 8.

Having optimized the conditions for $3\mathbf{R}$ synthesis in hand, the second step of the tandem reaction was studied without the isolation of $3\mathbf{R}$. First, reductive Heck coupling was carried out, in order to fabricate saturated non-symmetric ketone **6RR'**. Another portion of the aryl iodide **2R'** and the NPr₃ amine as a reducing agent were



FIGURE 8 Heck arylation between methyl vinyl ketone and psubstituted phenyl iodidesReaction conditions: 2.01 mmol 3-buten-2-one (MVK); 1.34 mmol ArI; 0.5 mol% Pd (OAc)2; 1.25 mmol NaHCO3; 1 hr; 120 °C; 2.5 cm3 DMF/H2O (3/2), MW; 0.5–3 bar

added to the reaction mixture obtained after the first Heck coupling (Figure 9).

During the reaction, the undesirable arylation of the remaining MVK by the aryl iodide **2R'** was also observed. To eliminate this side process, unreacted MVK was removed under vacuum before the introduction of the second aryl iodide. After this improvement, only two products were detected in the reaction mixture, namely **6RR'** and **4RR'**. Moreover, **6RR'** was the main one with the yield of 57–83% (Table 3).

Reactions were carried out in a mixture DMF/H_2O (3/2), and a total conversion of the aryl iodide 2R was achieved in all cases. It was found that the amount of NPr₃ influenced the product composition in reactions with p-iodoanisole, and a higher yield of **6RR'** was obtained in most cases using 1.58 mmol of amine than using 1.25 mmol. However, for p-iodotoluene, the amount of amine influenced the yield of **6RR'** much less.

In reactions with p-iodotoluene and iodobenzene, the final composition of the products was practically the same regardless of the order in which the reagents were added. Interestingly, in reactions with p-iodoanisole and iodobenzene, a much lower yield of **6RR'** (63%) was obtained when p-iodoanisole was used in the first step of the tandem reaction than in the second one (77%) (Table 3, runs 3 and 10). The E/Z ratio of **4RR'** isomers obtained in these reactions also differed from 16/15 to 13/8.

3.4 | Tandem synthesis of 4RR'

The process presented in Figure 9 led to the saturated non-symmetric ketone **6RR'** as the main product, while the unsaturated ketone **4RR'** was formed in a smaller



FIGURE 9 Synthesis of β , β -diaryl-2butanones under MW conditions in the presence of NPr3

TABLE 3 Results of tandem Heck reactions with different aryl iodides and NPr₃ as a reducing agent

Entry	NPr ₃ [mmol]	R	R'	Conversion 3R [%]	t [h]	6RR' [%]	4RR'(E/Z) [%]
1	1.25	Н	OMe	94	2	57	24/13
2	1.25	Н	OMe	95	3	69	19/7
3	1.58	Н	OMe	98	3	77	13/8
4	1.25	Н	Me	100	3	83	11/6
5	1.58	Н	Me	100	3	81	12/7
6	1.25	Me	Н	95	3	82	9/4
7	1.58	Me	Н	96	3	80	8/8
8	1.25	Me	OMe	98	3	69	10/19
9	1.58	Me	OMe	100	3	76	10/14
10	1.58	OMe	Н	94	3	63	16/15

Reaction conditions: **Step I:** 2.01 mmol 3-buten-2-one 1.34 mmol ArI – 2R; 0.5 mol% Pd (OAc)₂; 1.25 mmol NaHCO₃; 1 hr; 120 °C; 2.5 cm³ DMF/H₂O = 3/2; MW; 0.5–3 bar

Step II: 1.34 mmol ArI-2R', 120 °C; 2-3 hr; MW

quantity. In the next step of our studies, attempts were undertaken to reverse the reaction selectivity by changing the reaction conditions.

Two different protocols were tested for this purpose (Figures 10 and 11). In both of them, the substrate **3R** was obtained according to an optimized procedure with MW irradiation with a yield of 94%. Under the first method, **4RR'** was prepared using conventional heating (Figure 10). It was found that the formation of the unsaturated ketone **4RR'** is strongly dependent on the kind of base, and in these experiments carbonates of group I elements were used. In contrast to amines, carbonates have no reducing properties, and they therefore promoted the formation of Heck products, **4RR'**.



FIGURE 10 Synthesis of 4-(4methoxyphenyl)-4-phenyl-3-buten-2-ones with conventional heating in the presence of an inorganic base



FIGURE 11 Synthesis of β , β -diaryl-3buten-2-ones under MW conditions in the presence of a K2CO3 base

The introduction of a new portion of the base and piodoanisole to the DMF/H₂O solution containing **3R** obtained in the first step and heating it for *ca*. 16 hr made it possible to obtain **4RR'** in a moderate to very good yield (Figure 10, Table 4). The data presented in Table 4 show that potassium bases were better that sodium ones, and K_2CO_3 was superior to KHCO₃. Very similar results, *ca*. 80% of **4RR'**, were obtained in DMF/H₂O mixtures in 4/1 and 3/2 ratios. The yield of **6RR'** was as low as 3– 8%. The desired product, **4RR'**, was obtained with good yield in the tandem reaction presented in Figure 10; however, the second step of this process was relatively slow and reaction time as long as 16 hr was needed. Therefore, an improvement of this procedure was tested based on using MW irradiation in both steps (Figure 11).

As can be concluded from the data presented in Table 5, the coupling of 3R with p-iodoanisole was quite efficient and, already after 2 hr, 97% of **4RR'** was obtained (Table 5, entry 1). When 3R reacted with p-iodotoluene, a lower yield of **4RR'**, 69%, was achieved after 2 hr. It increased to 87% when a larger amount of K₂CO₃ was used (Table 5, entry 4). Even better results, 95% of **4RR'**, were obtained after 3 hr of the reaction (Table 5, entry 3). Interestingly, the introduction of iodide substrates in a reversed order (R = Me, R' = H) gave a lower yield of **4RR'** (94%) was

TABLE 4 The effect of different inorganic bases on the yield of4RR' in tandem Heck arylation

DMF/H ₂ O	Conversion 3R [%]	Base	4RR'(E/Z) [%]	6RR' [%]
4/1	22	NaHCO ₃	11/7	4
4/1	54	KHCO ₃	34/16	4
4/1	85	K ₂ CO ₃	56/26	3
3/2	86	K_2CO_3	52/26	8

Reaction conditions: **Step I:** 1.34 mmol ArI-2R; 1.34 mmol 3-buten-2-one; 0.5 mol% Pd (OAc)₂; 1.25 mmol NaHCO₃; 120 °C; 6 hr

Step II: 1.34 mmol ArI-2R'; 1.25 mmol base, 120 °C; 16 hr

TABLE 5 Results for tandem Heck reactions with different aryl iodides and a K₂CO₃ base

Entry	K ₂ CO ₃ [mmol]	R	R'	Conversion 3R [%]	t [h]	4RR'(E/Z) [%]	6RR' [%]
1	1.25	Н	OMe	100	2	65/32	3
2	1.25	Н	Me	71	2	49/20	2
3	1.25	Н	Me	95	3	61/34	-
4	1.58	Н	Me	89	2	55/32	2
5	1.25	Me	Н	75	2	29/46	-
6	1.25	Me	Н	73	3	30/43	-
7	1.25	Me	OMe	66	2	18/45	3
8	1.25	Me	OMe	94	3	33/61	-

Reaction conditions: **Step I**: 1.34 mmol ArI-2R; 2.01 mmol 3-buten-2-one; 0.5 mol% Pd (OAc)₂; 1.25 mmol NaHCO₃; 120 °C; 1 hr; DMF/H₂O = 3/2; MW, 0.5–3 bar

Step II: 1.34 mmol ArI-2R'; 120 °C; 2-3 hr; MW

obtained when R = Me and R' = OMe, indicating the electronic effect of the substituents (Table 5, entry 8).

Considering the stereoselectivity, E/Z ratio for **4RR'** isomers changed when the order of iodides introduction was changed. In the reaction with R = H and R' = Me the isomer E dominated and E/Z ratio was equal ca. 2 (Table 5, entry 2–4). However in the reverse sequence, with R = Me and R' = H, E/Z ratio was lower than 1 (Table 5, entry 5,6). Thus, the structure of intermediate **3R** (E) was not preserved during the second arylation performed according to Figure 11. In contrast, the E isomer was formed as the main one under conditions presented on Figure 9. The mixtures of stereoisomers were also obtained in chalcones arylation with Pd (OAc)₂ and P(o-Tol)₃.^[1]

4 | CONCLUSIONS

New, efficient palladium-catalyzed tandem methods for the preparation of 4,4-diarylbutanones and 4,4-diaryl-3butenones using MW heating have been developed. Each of the methods consists of two reactions proceeding one after the other in the same vessel with the same ligand-free catalyst and with 4-aryl-3-buten-2-one (3R) as an intermediate.

Advantageously, high yields of non-symmetric diarylketones were obtained in 2–3 hr from methyl vinyl ketone and aryl iodides without the isolation of **3R**. The reactions were catalyzed by Pd (OAc)₂ (0.5 mol%) without additional ligands or additives. For comparison, the arylation of MVK with iodobenzene was completed (74–83%) in 24 hr at 100 °C using conventional heating.^[19] The positive effect of MW in the conjugate addition and the Heck coupling was only shortly noted earlier.^[27] Recently arylation of chalcones was completed in 8 h using Pd (OAc)₂ and P(o-Tol)₃^[1]

Similarly to other authors, we observed that the selectivity of the second arylation depended on the type of base used. Tertiary amines (NPr₃; NBu₃; $(iPr)_2NEt$) directed the reaction towards saturated non-symmetric ketones (**6RR'**), whereas inorganic bases (NaHCO₃, KHCO₃ or K₂CO₃) promoted the formation of corresponding unsaturated ketones (**4RR'**). It can be assumed that amine acted as a hydrogen-transfer agent or a hydrogen source facilitating formation of the saturated product. In contrast, inorganic bases do not participate in hydrogen activation and in hydrogenation of unsaturated ketones.

Interestingly, the order of addition of aryl iodides in the tandem reaction has a significant effect on the amount of the desired product **6RR'**. In reactions with p-iodoanisole and PhI, the yield was 63% when PhI was used in the first step, while 77% of the same product was formed when p-iodoanisole was used as the first aryl iodide. The order of addition of aryl iodides influenced also the stereoselectivity of the second arylation.

During the first step of the catalytic reaction the color of the reaction mixture has changed from yellow to dark red and small amount of black precipitate, most probably containing palladium nanoparticles, was formed. Since the system was catalytically active in the second arylation, participation of palladium nanoparticles in the catalytic process should be seriously considered. The similar conclusion was formulated in our earlier studies on MVK arylation using the ligand-free palladium system.^[19]

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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