EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201300594

Facile One-Pot Palladium-Catalyzed Sequential Coupling to Diarylmethanes by Using Aryl Methyl Ketones as the Methylene Donors

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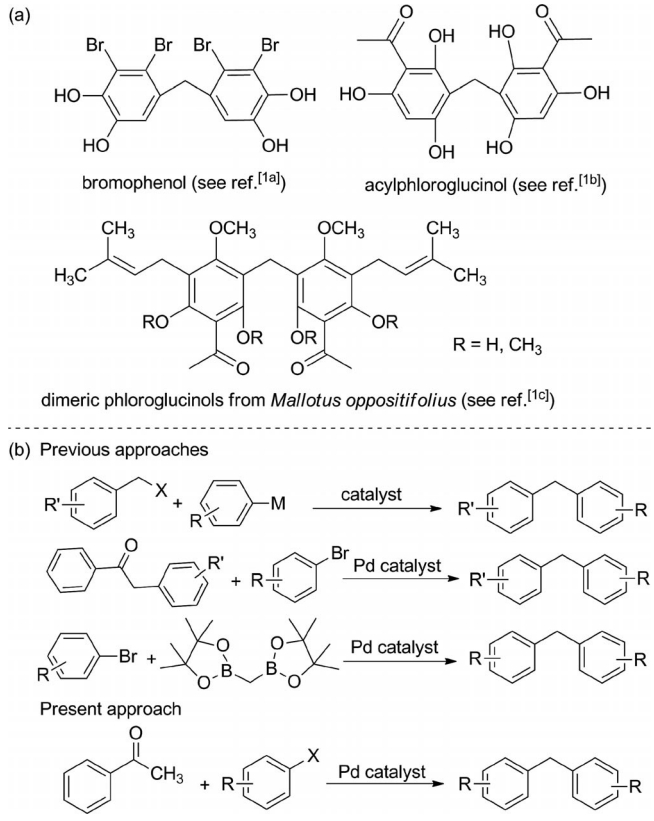
Keywords: Homogeneous catalysis / Palladium / Cross-coupling / C–C coupling / Reaction mechanisms

A novel palladium-catalyzed coupling reaction of an aryl methyl ketone with two molecules of an aryl halide to yield symmetric diarylmethanes is described. In the facile one-pot reaction, the aryl methyl ketone acts as a formal methylene donor. The experimental facts, including TLC monitoring, speculated intermediates as the raw materials, analysis of the cesium benzoate coproduct by ex situ IR spectroscopy, and the cross-coupling reactions of two different aryl halides, indicate a mechanism involving a palladium-catalyzed sequential two-step coupling process, in which the presence of a trace amount of H_2O is indispensable. The reaction is applicable to a broad spectrum of substrates and delivers the products in good to excellent yields. Access to unsymmetrical diarylmethanes with this method is also explored and various factors are discussed.

Introduction

Diphenylmethane is an important substructure unit that is found not only in a number of natural products[1] (representatives are shown in Scheme 1, a) but also in many synthetic compounds of biological and pharmaceutical importance.[2] Significant efforts are devoted to the construction of this motif and its derivatives, and diverse synthetic methods, roughly classified as conventional[3] and catalytic,[4] have been reported so far. In the past decade, catalytic methodologies have received great attention because of their high efficiency and because they can be easily used for the construction of generally inaccessible diphenylmethane derivatives through C–C bond formation.[4a,4k,5–7] For example, the palladium-catalyzed coupling of benzyl halides with aryl nucleophiles[5] and the α-arylation of diphenylethanones with aryl bromides[6] are among the most effective methods used to prepare this distinct class of compounds. Another interesting example was reported recently in which air-stable diborylmethane was coupled with aryl bromides (2 equiv.) by using palladium catalysis for the synthesis of various diarylmethanes (Scheme 1, b).[7]

The common feature in the mechanism of the palladium-catalyzed α-arylation of carbonyl compounds is a one-cycle process involving successive oxidative addition, transmetalation, and reductive elimination,[8] and the equilibrium between the Pd–O and Pd–C species in the transmetalation step can be the rate-determining step.[9] Several factors de-



Scheme 1. (a) Several naturally occurring compounds containing the diphenylmethane unit. (b) Reported methods for constructing diphenylmethane compounds and the method developed herein.

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201300594.

termine the success of the reaction, including the ligand(s) of the palladium complex; the nature of the aryl halide, carbonyl compound, base, and solvent; the stoichiometry of the reagents; and the reaction temperature.

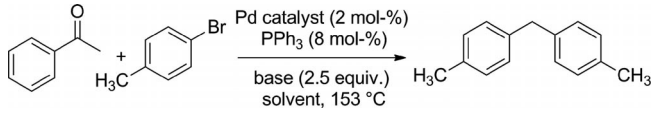
Most of the reported works are devoted to the design of the palladium catalysts. Our initial effort was focused on the direct coupling reaction of acetophenone with substituted bromobenzene to yield various 1,2,2-triphenylethanones by using $PdCl_2$ as the catalyst, which can usually be accomplished under anhydrous and inert atmosphere conditions.[10] On one occasion in which the reaction was conducted without dry DMF or the protection of an inert atmosphere, to our surprise, the direct α,α-diarylation of acetophenone to 1,2,2-triphenylethanone was not achieved, but instead diphenylmethane was generated. Given that the methylene group must come from acetophenone, acetophenone formally functions as the methylene donor, and hence, the product, diphenylmethane, seems to be the result of the cleavage of 1,2,2-triphenylethanone at the benzoyl site in the presence of a trace amount of water in the reaction medium. Remarkably, this kind of reaction has not been reported to date. It may be viewed as a new method for the synthesis of diarylmethanes, and the reaction scope and mechanism deserve to be further investigated.

In this article, we report the investigation of this unusual reaction by screening the optimal reaction conditions of the direct coupling of acetophenone with 4-bromobenzene to the symmetric diarylmethane product, bis(4-methylphenyl)-methane, and then we expand the substrate scope and offer insight into the mechanism. Finally, access to unsymmetrical diarylmethanes with this method is also explored.

Results and Discussion

First, optimization of the reaction conditions was performed on the model coupling reaction of 4-bromotoluene with acetophenone for the synthesis of di-*p*-tolylmethane. Selected results are shown in Table 1. The isolated product was obtained in up to 80% yield with an acetophenone/4-bromotoluene ratio of 1:2 under reflux and the catalysis of $PdCl_2$ and PPh_3 (Table 1, entry 1). Upon lowering the temperature to 60 °C, no reaction occurred (Table 1, entry 2). No product was observed if KOH, K_2CO_3, or NaO*t*Bu was used as the base (Table 1, entry 3). Both $K_3PO_4{\cdot}3H_2O$ and Cs_2CO_3 promoted the reaction, but Cs_2CO_3 was more efficient (Table 1, entries 1 and 4). Upon conducting the reaction in the presence of 2.5 equiv. Cs_2CO_3, the highest yield was obtained (Table 1, entries 1 and 5). However, changing the solvent from DMF to another one, such as THF and toluene, shut down the reaction completely (Table 1, entry 6). In addition, the use of H_2O as the solvent and tetrabutylammonium bromide (TBAB) as the phase-transfer agent decreased the reaction yield dramatically (Table 1, entry 7). Moreover, by replacing PPh_3 with dicyclohexyl(2-mesityl-1*H*-inden-1-yl)phosphane as the spectator ligand,[11] the yield decreased to 10% (Table 1, entry 8), which suggests that the bulky phosphane ligand suppressed the reaction, and this is similar to the result obtained in the α-diarylation of ketones reported by Palucki.[12] The catalytic system of $Pd(OAc)_2$ (2 mol-%) and PPh_3 (8 mol-%) delivered the product in 82% yield (Table 1, entry 9), whereas the use of $Pd_2(dba)_3$ (dba = dibenzylideneacetone) as the catalyst resulted in a decrease in the yield to 56% (Table 1, entry 10). The yield decreased to 59% (Table 1, entry 1) if a larger amount of bromobenzene was used and to 38% (Table 1, entry 9) if a higher catalyst loading was applied, probably because of over-reaction. In the former case, triarylmethane[13] may be produced, whereas in the latter case, oxidation of diarylmethane to diarylmethanone[14] is possible. Therefore, the optimum reaction conditions for the synthesis of diarylmethanes involved the use of DMF as the solvent in the presence of $Pd(OAc)_2$ (2 mol-%), PPh_3 (8 mol-%), and Cs_2CO_3 (2.5 equiv.) under reflux (ca. 153 °C).

Table 1. Conditions for the synthesis of di-*p*-tolylmethane.[a]



Entry	Catalyst[b]	Base[b]	Solvent	Yield[c] [%]
1	$PdCl_2$	Cs_2CO_3	DMF	63/80/59[d]
2	$PdCl_2$	Cs_2CO_3	DMF	0/3[e]
3	$PdCl_2$	KOH, K_2CO_3, or NaO*t*Bu	DMF	0
4	$PdCl_2$	$K_3PO_4{\cdot}3H_2O$	DMF	59
5	$PdCl_2$	Cs_2CO_3	DMF	33/69/67[f]
6	$PdCl_2$	Cs_2CO_3	THF or toluene	0
7	$PdCl_2$	Cs_2CO_3	H_2O[g]	23
8	$PdCl_2$[h]	Cs_2CO_3	DMF	10
9	$Pd(OAc)_2$	Cs_2CO_3	DMF	13/82/38[i]
10	$Pd_2(dba)_3$	Cs_2CO_3	DMF	56

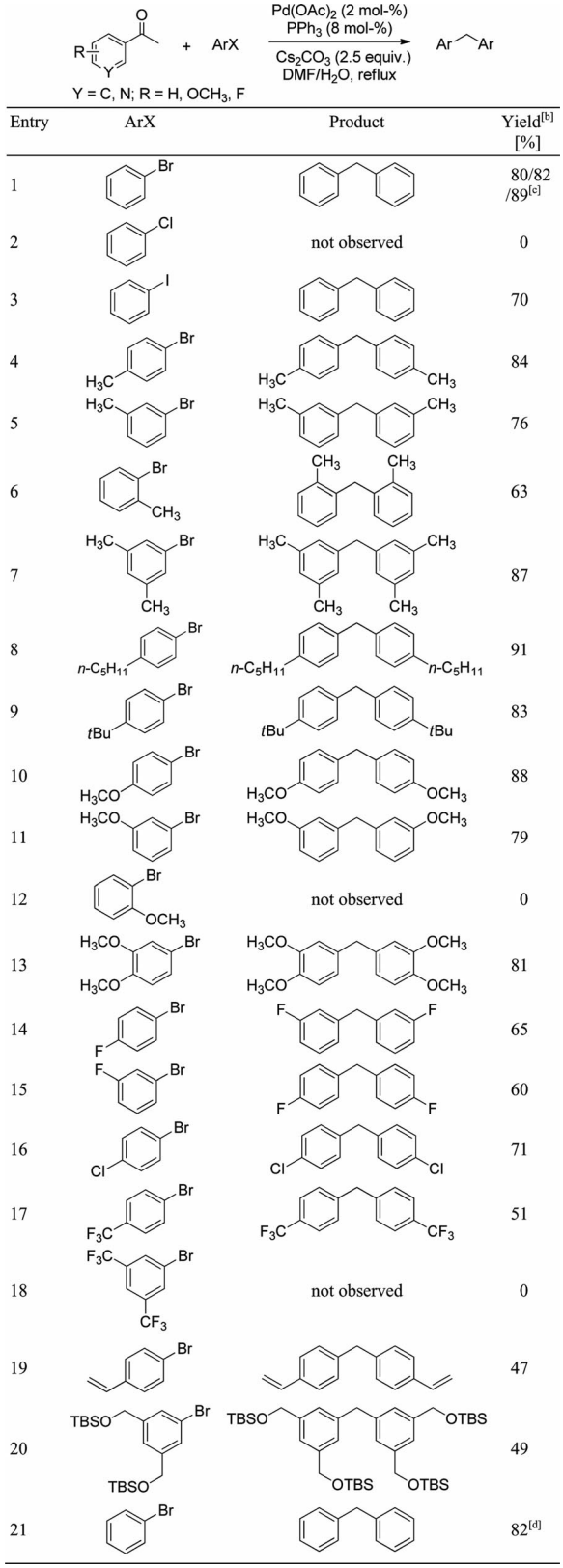
[a] Reactions were conducted with acetophenone (3.1 mmol) and 4-bromotoluene (6.2 mmol) in solvent (20 mL) for 8 h. All ratios of the substrates were 1:2 unless otherwise noted. [b] Loading based upon acetophenone. [c] Yield of isolated product. [d] Yield obtained with a substrate ratio of 1:1, 1:2, and 1:3.4, respectively. [e] Yield obtained by conducting the reaction at 60 and 120 °C, respectively. [f] Yield obtained by using 1.0, 2.0, and 3.0 equiv. of Cs_2CO_3, respectively. [g] TBAB (1.55 mmol) was added. [h] Dicyclohexyl(2-mesityl-1*H*-inden-1-yl)phosphane was used as the ligand. [i] Yield obtained by using 1+4, 2+8, and 4+16 mol-% of $Pd(OAc)_2$ + PPh_3, respectively.

To probe the substrate scope of the reaction, various aryl methyl ketones were used to react with a broad range of aryl halides under the optimum conditions, and the results are listed in Table 2. Aryl methyl ketones, with little influence from the substituent on the aryl group, efficiently coupled with phenyl bromide (Table 2, entry 1). Among the phenyl halides tested, the bromide was the most efficient (Table 2, entries 1–3), which is consistent with the results of the α,α-diarylation of acetophenones.[8d] The nature of the substituents on the aryl halide had a pronounced impact on the yield, and electron-rich substituents (Table 2, entries 4–11 and 13) performed better than electron-deficient

ones (Table 2, entries 14–19). For example, upon treatment of acetophenone with 3,5-bis(trifluoromethyl)phenyl bromide, no desired product was observed (Table 2, entry 18), whereas upon treatment with 4-trifluoromethylphenyl bromide, a moderate yield was obtained (Table 2, entry 17). For an aryl bromide with *ortho* steric hindrance or a *para* long-chain substituent, the yield was 63 or 91%, respectively (Table 2, entries 6 and 8). Furthermore, upon coupling acetophenone with 4-bromochlorobenzene, selective production of bis(4-chlorophenyl)methane was observed (Table 2, entry 16). Importantly, some aryl halides with functional groups were able to give the corresponding diarylmethanes in moderate yields (Table 2, entries 19 and 20). For example, 4-bromostyrene coupled with acetophenone to produce bis(4-vinylphenyl)methane in 47% yield, whereas *tert*-butyldimethylsilyl (TBS)-protected 3,5-di(hydroxymethyl)phenyl bromide reacted with acetophenone to give bis[3,5-di(*tert*-butyldimethylsilyloxymethyl)phenyl]methane, which can be conveniently deprotected to give the corresponding polyhydroxy-bearing diarylmethane (Table 2, entry 20). However, for an aryl bromide with a 2-methoxy group (Table 2, entry 12) or an active hydrogen such as that in the amino and hydroxy groups (data not shown), no coupling product was obtained. Interestingly, 3-acetylpyridine, a heteroaryl methyl ketone, was also able to function as the methylene donor to achieve diphenylmethane in good yield (Table 2, entry 21).

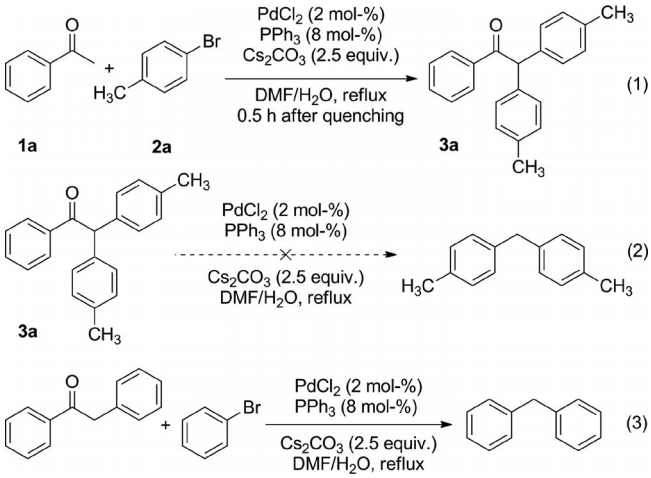
Notably, if the reaction of acetophenone with phenyl bromide was carried out under anhydrous conditions, the normal α-arylation product, diphenylethanone, was obtained, as reported by Churruca,[15] without the formation of diphenylmethane. It was speculated that the presence of H_2O was indispensable. To understand this reaction performed without the use of dry DMF or the protection of an inert atmosphere, the progress was first checked by TLC monitoring. A major new spot appeared on the TLC plate after a reaction time of 0.5 h, which gradually disappeared as time progressed. Normal product **3a**, resulting from the α,α-diarylation of acetophenone, was obtained by quenching the reaction after 0.5 h [Scheme 2, Eq. (1)]. Upon completion of the reaction, however, di-*p*-tolylmethane instead of **3a** was obtained. No di-*p*-tolylmethane was observed if **3a** as the raw material was added to the reaction mixture under the same conditions [Scheme 2, Eq. (2)], which suggests that **3a** was not the real intermediate and that the spot that appeared on the TLC plate might come from an unknown key intermediate, which may transform into **3a** during chromatography or upon quenching the reaction with 1.4 M HCl after 0.5 h. However, if 1,2-diphenylethanone was used in the reaction with bromobenzene, the desired diphenylmethane was obtained [Scheme 2, Eq. (3)], and consequently, 1,2-diphenylethanone was another key intermediate. 1,2-Diphenylethanone is a benzyl-type ketone, and α-arylation has been reported, such as the palladium-catalyzed α-arylation of benzyl ketone with iodobenzene[16] and, more similarly, that of 1,2-diphenylethanone with various aryl bromides for the synthesis of diarylmethanes in aqueous media with microwave heating.[6]

Table 2. Substrate scope for the synthesis of diarylmethanes.[a]



Entry	ArX	Product	Yield[b] [%]
1			80/82 /89[c]
2		not observed	0
3			70
4			84
5			76
6			63
7			87
8			91
9			83
10			88
11			79
12		not observed	0
13			81
14			65
15			60
16			71
17			51
18		not observed	0
19			47
20			49
21			82[d]

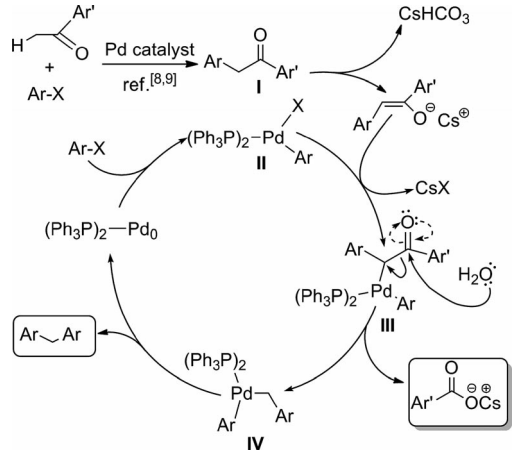
[a] Conditions: Aryl methyl ketone (3.1 mmol), aryl halide (6.2 mmol) for about 12 h. [b] Yield of isolated product. [c] 4-Fluoroacetophenone, 4-methoxyacetophenone, or acetophenone was used as the methylene donor, respectively. [d] 3-Acetylpyridine was used as the methylene donor.



Scheme 2. Reaction equations for mechanism exploration.

The above model reactions preliminarily demonstrated that there may be two key intermediates involved in the reaction: one is 1,2-diphenylethanone, whereas the another remains unknown. In the α,α-diarylation of acetophenone with aryl bromide to give **3a** [Scheme 2, Eq. (1)], Churruca et al. performed a detailed investigation and suggested a key intermediate Pd^{II} complex bearing aryl and diarylethanon-α-yl groups under the anhydrous conditions that transforms into triarylethanone **3a** after water workup.[10] As mentioned above, **3a** was unable to be transformed into diarylmethane in our case, which demonstrates that the reaction of this Pd^{II} complex to give **3a** is an irreversible process. Given that the present reaction was conducted in wet DMF, a water-mediated process for the transformation of the Pd^{II} complex into the diarylmethane is possible. The process may occur by water attack at the carbonyl of the diarylethanon-α-yl group, and this would lead to the generation of an unreported intermediate and the release of a coproduct, $ArCO_2Cs$. Notably, this unreported intermediate is likely the phenylmethylene-bound Pd species with phenyl attached simultaneously. Then, this intermediate may further transform into the diarylmethane by reductive elimination. The distinct feature of this transformation is the water-mediated C–C activation. Similarly, water-mediated C–C activation in the α-arylation of β-dicarbonyl compounds to aryl ketones has been reported by Lei and colleagues.[17]

Therefore, a complete mechanism involving a catalytic two-cycle process is proposed for the reaction and is shown in Scheme 3. At first, the α-arylation of acetophenone with the palladium catalyst to give diarylethanone **I** is included in the first cycle, which has been well documented in a number of publications.[8,9] Next, diarylethanone **I** enolizes and couples to Pd^{II} complex **II** generated from the Pd^0 precatalyst by oxidative addition of ArX in the reaction to form intermediate **III**. Intermediate **III** then undergoes reductive elimination, and after acidic aqueous workup, affords triphenylethanone **3a** as the normal reported process.[10] However, in our case, a trace amount of H_2O may attack the carbonyl group of intermediate **III** before reductive elimination occurs, which leads to cleavage of the C–C bond and the formation of intermediate **IV**. A necessary indicator of this process should be the concomitant product $ArCO_2Cs$. Intermediate **IV** undergoes reductive elimination to generate the desired diarylmethane and the active Pd^0 species for the next catalytic cycle. The whole mechanism involves a one-pot palladium-catalyzed sequential two-step coupling process.



Scheme 3. The proposed mechanism.

The indicator, the concomitant product $ArCO_2Cs$ (in this case, cesium benzoate), may be used to support this proposed mechanism. Thus, the reaction mixture was acidified, extracted, and subjected to column chromatography, and finally benzoic acid was indeed obtained and identified. With this knowledge, the reaction mixture was sampled at an interval of 1 h and the in situ formation of $PhCO_2Cs$ was analyzed by IR spectroscopy by comparing the measured spectra to the standard spectrum of $PhCO_2Cs$ (Figure 1). The characteristic bands of $PhCO_2Cs$ centered at approximately 1558 (C=O stretch of benzoate) and 715 cm^{-1} (one of the C–H out-of-plane bendings of monosubstituted benzene) and their intensities increased as time progressed, which is suggestive of the continuous generation of $PhCO_2Cs$ in the reaction direction of the proposed mechanism.

According to this mechanism, if two mixed aryl halides were used simultaneously, three cross-coupling products could be possible (Scheme 4, a). For example, simultaneous treatment of acetophenone with bromobenzene and 4-bromotoluene under our conditions resulted in the formation of three different diarylmethanes, as recognized by characteristic resonances for the methylene unit in the ^1H NMR spectrum (Scheme 4, b, top). Two of the three diarylmethanes were identified as diphenylmethane and di-*p*-tolylmethane by comparing the characteristic chemical shifts of the methylene group to the methylene signals of pure diphenylmethane (Table 2, entry 1) and di-*p*-tolylmethane (Table 2, entry 4). The remaining methylene signal at δ = 3.935 ppm, with the highest intensity lying in between the two known diarylmethanes, should be the characteristic resonance for the methylene group of the unsymmetrical *p*-tolylphenylmethane product.

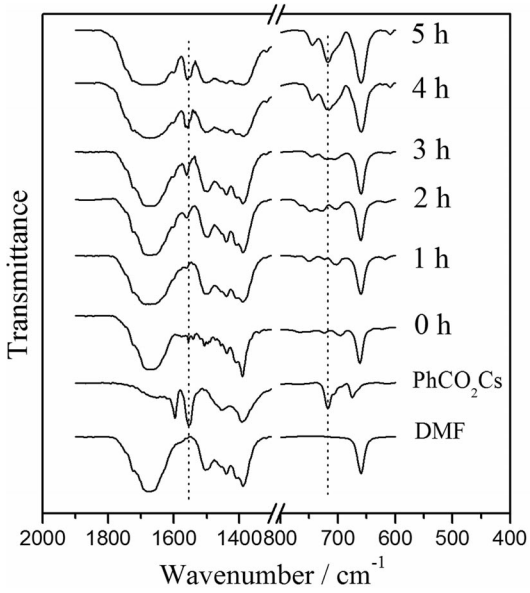
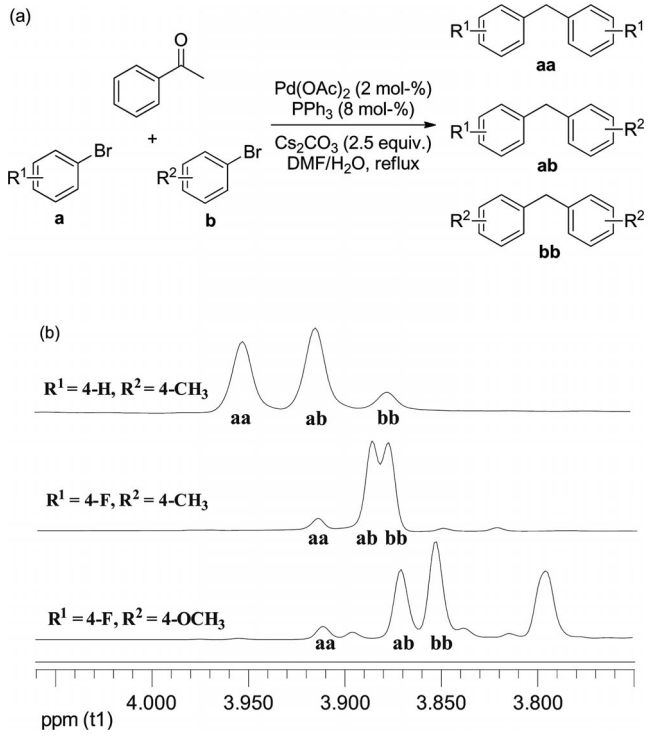


Figure 1. IR spectra of samples at different reaction times, together with that of the solvent DMF and pure cesium benzoate.



Scheme 4. (a) Predicted products for the one-pot cross-coupling reaction. (b) ^{1}H NMR spectra in the region of 4.06–3.75 ppm for the mixtures obtained from the one-pot cross-coupling reactions.

To inspect the cross-coupling reactivity of different aryl halides, two other cross-coupling reactions were conducted, that is, the reaction of 4-fluorophenyl bromide with 4-bromotoluene and the reaction of 4-fluorophenyl bromide with 4-methoxyphenyl bromide, and the pairs in these reactions have relatively large differences in the electronegativity of the substituent. Each reaction produced a mixture of three diarylmethanes (Scheme 4, b, middle and bottom), and the compositions were also identified by the above method. The different integration of the methylene resonances is indicative of their relative abundance, which evidences that 4-bromotoluene and 4-methoxyphenyl bromide tend to undergo self-coupling, whereas 4-fluorophenyl bromide tends to undergo cross-coupling. It is known that electron-deficient aryl halides form diarylethanones more easily,[8c] as intermediate **I** in the first cycle in our proposed mechanism leads to a more stable enolate through stabilization by the electron-deficient substituent. However, in the second cycle, it is reasonable that the electron-rich aryl halide will tend to have higher reactivity in the oxidative addition to form intermediate **II**. Thus, the following transmetalation, water-mediated C–C cleavage, and reductive elimination give high yields for the self-coupling product of an electron-rich aryl halide and for the cross-coupling product of an electron-rich aryl halide and an electron-deficient one and a very low yield for the self-coupling product of an electron-deficient aryl halide.

The above-obtained mixtures were subjected to column chromatography. However, because of the small differences in the polarities of the individual components, isolation of the cross-coupling product derived from bromobenzene and 4-bromotoluene as well as that derived from 4-fluorophenyl bromide and 4-bromotoluene failed. However, cross-coupling 4-fluoro-4′-methoxydiphenylmethane product derived from 4-fluorophenyl bromide and 4-methoxyphenyl bromide was isolated in 40% yield, and its structural information is described in the Experimental Section.

Cross-coupling reactions for the synthesis of various unsymmetrical diarylmethanes are also possible; nevertheless, precaution should be taken. Given that the sequential two-step coupling reaction is a successive process, a strategy should be adapted to stop the reaction at the stage of the formation of intermediate **I** after the first cycle so that the first aryl halide will not participate in the second catalytic cycle and that the second aryl halide will not participate in the first catalytic cycle. In one of the above examples, by making use of the different polarities and activities of the substituents on the coupling aryl halide pair, it is possible to obtain the cross-coupling product, although in relatively low yield.

Conclusions

In summary, we report the first examples of the synthesis of symmetrical diarylmethanes by facile, one-pot, two-step, palladium-catalyzed sequential coupling. The method is also applicable to the synthesis of unsymmetrical diarylmethanes through a cross-coupling reaction. The major advantage of this synthesis over the state-of-the-art methods is the utilization of aryl methyl ketones as the methylene donors, as they are cheap and widely available. The use of a palladium catalyst without the need of a complex and specially designed ligands is another valuable merit. A plausible mechanism was outlined in detail, and it was sup-

ported by the following experimental facts: TLC monitoring, intermediates possible as the raw materials, analysis of the cesium benzoate coproduct by ex situ IR spectroscopy, and the result of the cross-coupling model reaction.

Experimental Section

General Information: Unless otherwise noted, materials were used as commercially supplied. All reactions were monitored by TLC analysis on silica gel coated plates. Flash column chromatography was performed by using 200–300 mesh silica gel. ^{1}H NMR spectra were recorded with Varian Mercury 400 or 600 MHz spectrometers. Chemical shifts (δ) are reported in ppm from tetramethylsilane (internal standard, 0.0 ppm). ^{13}C NMR spectra were recorded with the same spectrometers operating at 100 and 150 MHz, respectively, with complete proton decoupling (internal standard $CDCl_3$: 77.0 ppm). IR measurements were performed with a Bruker TENSOR27 by using KBr pellets. Mass spectra were measured with a Finnigan Trace MS spectrometer. Elementary analysis was taken with a Vario EL III elementary analysis instrument.

α,α-Bis(4-methoxyphenyl)acetophenone: DMF (20 mL) was added to a round-bottomed flask charged with Cs_2CO_3 (2.53 g, 7.75 mmol), PPh_3 (65.05 mg, 0.248 mmol), $PdCl_2$ (10.99 mg, 0.062 mmol), acetophenone (0.37 g, 3.1 mmol), and 4-bromotoluene (1.06 g, 6.2 mmol) at room temperature. The resulting suspension was stirred and heated to 153 °C for 0.5 h. After cooling, HCl (1.4 M in H_2O, 50 mL) was added, and the aqueous layer was extracted with CH_2Cl_2 (3× 30 mL). The combined organic extract was washed with saturated aqueous NH_4Cl (3× 100 mL), dried with anhydrous sodium sulfate, and concentrated in vacuo to give a residue. The residue was purified by column chromatography on silica gel (petroleum ether) to give the product as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, J = 7.6 Hz, 2 H), 7.49 (t, J = 7.6 Hz, 1 H), 7.37–9.41 (m, 2 H), 7.10–7.16 (m, 8 H), 5.96 (s, 1 H), 2.30 (s, 6 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 198.43, 136.78, 136.61, 136.21, 132.84, 129.35, 128.88, 128.49, 128.24, 58.65, 21.01 ppm. $C_{22}H_{20}O$ (300.40): calcd. C 87.96, H 6.71; found C 87.71, H 6.64.

Benzoic Acid: DMF (20 mL) was added to a round-bottomed flask charged with Cs_2CO_3 (2.53 g, 7.75 mmol), PPh_3 (65.05 mg, 0.248 mmol), $Pd(OAc)_2$ (13.92 mg, 0.062 mmol), acetophenone (0.37 g, 3.1 mmol), and 4-bromotoluene (1.06 g, 6.2 mmol) at room temperature. The resulting suspension was stirred and heated to 153 °C, and the progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was cooled. HCl (1.4 M in H_2O, 50 mL) was added, and the aqueous layer was extracted with CH_2Cl_2 (3× 100 mL). The combined organic layer was alkalified to pH 11 by using NaOH (aq.). The water phase was separated and acidified to pH 3. The combined liquid layer was extracted with CH_2Cl_2 (3× 10 mL) and dried with anhydrous sodium sulfate, and the solvents were evaporated in vacuo to give a residue. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to give the product as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.3 (s, 1 H), 8.13 (d, J = 7.2 Hz, 2 H), 7.63 (t, J = 7.6 Hz, 1 H), 7.47–7.51 (m, 2 H) ppm.

General Procedure for the Synthesis of Diarylmethanes: DMF (20 mL) was added to a round-bottomed flask charged with Cs_2CO_3 (2.53 g, 7.75 mmol), PPh_3 (65.05 mg, 0.248 mmol), $Pd(OAc)_2$ (13.92 mg, 0.062 mmol), one ketone (3.1 mmol), and an aryl halide (6.2 mmol) at room temperature. The resulting suspension was stirred and heated to 153 °C, and the progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was cooled. HCl (1.4 M in H_2O, 50 mL) was added, and the aqueous layer was extracted with CH_2Cl_2 (3× 30 mL). The combined organic extract was washed with saturated aqueous NH_4Cl (3× 100 mL), dried with anhydrous sodium sulfate, and concentrated in vacuo to give a residue. Then, the residue was purified by column chromatography on silica gel (petroleum ether or petroleum ether/ethyl acetate) to give the product. All the as-synthesized diarylmethanes are listed in Table 2.

Diphenylmethane: The ketone (3.1 mmol; acetophenone, 0.37 g; 4-methoxyacetophenone, 0.47 g; 4-fluoroacetophenone, 0.43 g; or 3-acetylpyridine, 0.38 g) and an aryl halide (6.2 mmol; bromobenzene, 0.97 g; iodobenzene, 1.27 g) were used. The product was obtained as a colorless oil. The yields are indicated in Table 2, entry 1 (0.424 g, 80%; 0.435 g, 82%; 0.472 g, 89%) and entry 21 (0.435 g, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17–7.29 (m, 10 H), 3.97 (s, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 141.08, 128.91, 128.43, 126.03, 41.92 ppm. MS: m/z = 168.1 $[M]^+$. $C_{13}H_{12}$ (168.24): calcd. C 92.81, H 7.19; found C 92.63, H 6.99.

Di-*p*-tolylmethane: Acetophenone (0.37 g, 3.1 mmol) and 4-bromotoluene (1.06 g, 6.2 mmol) were used. The product was obtained as colorless oil (0.508 g, 82%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.06 (d, J = 9 Hz, 8 H), 3.89 (s, 2 H), 2.29 (s, 6 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.34, 135.38, 129.08, 128.72, 41.06, 20.98 ppm. MS: m/z = 196.1 $[M]^+$. $C_{15}H_{16}$ (196.29): calcd. C 91.78, H 8.22; found C 91.61, H 8.03.

Di-*m*-tolylmethane:[7] Acetophenone (0.37 g, 3.1 mmol) and 3-bromotoluene (1.06 g, 6.2 mmol) were used. The product was obtained as a colorless oil (0.464 g, 76%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.15–7.18 (m, 2 H), 6.98–7.01 (m, 6 H), 3.89 (s, 2 H), 2.30 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.13, 137.97, 129.67, 128.29, 126.75, 125.94, 41.84, 21.40 ppm. MS: m/z = 196.2 $[M]^+$.

Di-*o*-tolylmethane: Acetophenone (0.37 g, 3.1 mmol) and 2-bromotoluene (1.06 g, 6.2 mmol) were used. The product was obtained as a colorless oil (0.391 g, 63%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.20 (d, J = 6.6 Hz, 2 H), 7.14–7.16 (m, 2 H), 7.10–7.12 (m, 2 H), 6.89 (d, J = 6.6 Hz, 2 H), 3.92 (s, 2 H), 2.28 (s, 6 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.33, 136.49, 130.01, 129.09, 126.19, 126.00, 36.66, 19.54 ppm. MS: m/z = 196.2 $[M]^+$. $C_{15}H_{16}$ (196.29): calcd. C 91.78, H 8.22; found C 91.59, H 8.00.

Bis(3,5-dimethylphenyl)methane: Acetophenone (0.37 g, 3.1 mmol) and 3,5-dimethylbromobenzene (1.45 g, 6.2 mmol) were used. The product was obtained as a colorless oil (0.618 g, 87%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.82 (s, 2 H), 6.81 (s, 4 H), 3.81 (s, 2 H), 2.27 (s, 12 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 141.18, 137.83, 127.54, 126.64, 41.74, 21.73 ppm. MS: m/z = 224.2 $[M]^+$. $C_{17}H_{20}$ (224.35): calcd. C 91.01, H 8.99; found C 90.83, H 8.85.

Bis(4-pentylphenyl)methane: Acetophenone (0.37 g, 3.1 mmol) and 1-bromo-4-pentylbenzene (1.41 g, 6.2 mmol) were used. The product was obtained as a colorless oil (0.892 g, 91%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.08 (s, 8 H), 3.89 (s, 2 H), 2.55 (t, J = 11.4 Hz, 4 H), 1.56–1.62 (m, 4 H), 1.30–1.31 (m, 8 H), 0.88 (t, J = 10.8 Hz, 6 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 140.52, 138.50, 128.63, 128.34, 41.13, 35.52, 31.55, 31.26, 22.56, 14.16 ppm. MS: m/z = 308.3 $[M]^+$. $C_{23}H_{32}$ (308.51): calcd. C 89.54, H 10.46; found C 89.31, H 10.26.

Bis(4-*tert*-butylphenyl)methane:[18] Acetophenone (0.37 g, 3.1 mmol) and 1-bromo-4-*tert*-butylbenzene (0.32 g, 6.2 mmol) were used. The product was obtained as a colorless oil (0.714 g,

83%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.30 (d, J = 7.2 Hz, 4 H), 7.13 (d, J = 7.8 Hz, 4 H), 3.92 (s, 2 H), 1.29 (s, 18 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 148.69, 138.23, 128.51, 125.30, 40.89, 34.34, 31.39 ppm. MS: m/z = 280.4 $[M]^+$.

Bis(4-methoxyphenyl)methane: Acetophenone (0.37 g, 3.1 mmol) and 1-bromo-4-methoxybenzene (1.16 g, 6.2 mmol) were used. The product was obtained as a yellow oil (0.634 g, 88%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.08 (d, J = 7.8 Hz, 4 H), 6.82 (d, J = 8.4 Hz, 4 H), 3.86 (s, 2 H), 3.77 (s, 6 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 157.87, 133.69, 129.70, 113.82, 55.23, 40.09 ppm. MS: m/z = 228.1. $[M]^+$. $C_{15}H_{16}O_2$ (228.29): calcd. C 78.92, H 7.06; found C 79.09, H 6.93.

Bis(3-methoxyphenyl)methane:[7] Acetophenone (0.37 g, 3.1 mmol) and 3-bromoanisole (1.16 g, 6.2 mmol) were used. The product was obtained as a yellow oil (0.561 g, 79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20 (t, J = 7.6 Hz, 2 H), 6.79 (d, J = 7.6 Hz, 2 H), 6.74 (d, J = 6.0 Hz, 4 H), 3.92 (s, 2 H), 3.77 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.68, 142.46, 129.38, 121.34, 114.74, 111.33, 55.12, 41.96 ppm. MS: m/z = 228.2 $[M]^+$.

Bis(3,4-dimethoxyphenyl)methane:[6] Acetophenone (0.37 g, 3.1 mmol) and 1-bromo-3,4-dimethoxybenzene (1.34 g, 6.2 mmol) were used. The product was obtained as a yellow oil (0.721 g, 81%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.79 (s, 2 H), 6.71 (d, J = 15.6 Hz, 4 H), 3.88 (s, 2 H), 3.86 (s, 6 H), 3.83 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.80, 147.27, 133.81, 120.64, 112.01, 111.08, 55.82, 55.72, 40.90 ppm. MS: m/z = 288.3 $[M]^+$.

Bis(4-fluorophenyl)methane: Acetophenone (0.37 g, 3.1 mmol) and 1-bromo-4-fluorobenzene (1.09 g, 6.2 mmol) were used. The product was obtained as a colorless oil (0.423 g, 65%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.11 (t, J = 7.8 Hz, 4 H), 6.97 (t, J = 9 Hz, 4 H), 3.91 (s, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.21, 160.59, 136.55, 130.15, 115.33, 115.19, 40.18 ppm. MS: m/z = 204.1 $[M]^+$. $C_{13}H_{10}F_2$ (204.22): calcd. C 76.46, H 4.94; found C 76.28, H 4.87.

Bis(3-fluorophenyl)methane: Acetophenone (0.37 g, 3.1 mmol) and 1-bromo-4-fluorobenzene (1.09 g, 6.2 mmol) were used. The product was obtained as a colorless oil (0.378 g, 60%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.23 (t, J = 7.2 Hz, 2 H), 6.95 (d, J = 7.2 Hz, 2 H), 6.90 (d, J = 9.0 Hz, 2 H), 6.86 (t, J = 9.6 Hz, 2 H), 3.94 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.19, 161.74, 142.81, 142.74, 130.29, 129.92, 124.53, 124.50, 115.88, 115.66, 113.36, 113.15, 41.24 ppm. MS: m/z = 204.2 $[M]^+$. $C_{13}H_{10}F_2$ (204.22): calcd. C 76.46, H 4.94; found C 76.28, H 5.18.

Bis(4-chlorophenyl)methane: Acetophenone (0.38 g, 3.1 mmol) and 1-bromo-4-chlorobenzene (1.18 g, 6.2 mmol) were used. The product was obtained as a colorless oil (0.533 g, 71%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.24 (d, J = 8.4 Hz, 4 H), 7.07 (d, J = 7.8 Hz, 4 H), 3.89 (s, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.96, 132.07, 130.14, 128.63, 40.48 ppm. MS: m/z = 236.0 $[M]^+$. $C_{13}H_{10}Cl_2$ (237.13): calcd. C 65.85, H 4.25; found C 65.96, H 4.14.

Bis(4-trifluoromethylphenyl)methane: Acetophenone (0.38 g, 3.1 mmol) and 1-bromo-4-(trifluoromethyl)benzene (1.39 g, 6.2 mmol) were used. The product was obtained as a colorless oil (0.490 g, 51%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.55 (d, J = 7.8 Hz, 4 H), 7.28 (d, J = 7.8 Hz, 4 H), 4.07 (s, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 143.24, 129.23, 127.62, 125.93, 123.25, 41.43 ppm. MS: m/z = 304.0 $[M]^+$.

Bis(4-vinylphenyl)methane: Acetophenone (0.37 g, 3.1 mmol) and 4-bromostyrene (1.14 g, 6.2 mmol) were used. The product was obtained as a colorless oil (0.320 g, 47%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, J = 8.0 Hz, 4 H), 7.14 (d, J = 8.0 Hz, 4 H), 6.68 (q, J = 6.8 Hz, 2 H), 5.70 (d, J = 18 Hz, 2 H), 5.19 (d, J = 11.2 Hz, 2 H), 3.59 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.67, 136.55, 135.54, 129.05, 126.33, 113.23, 41.35 ppm. MS: m/z = 220.3 $[M]^+$. $C_{17}H_{16}$ (220.31): calcd. C 92.68, H 7.32; found C 92.87, H 7.56.

Bis[3,5-di(*tert*-butyldimethylsilyloxymethyl)phenyl]methane: Acetophenone (0.37 g, 3.1 mmol) and 3,5-di(*tert*-butyldimethylsilyloxymethyl)phenyl bromide (2.58 g, 6.2 mmol) were used. The product was obtained as a yellow oil (1.120 g, 49%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.15 (s, 2 H), 6.98 (s, 4 H), 4.68 (s, 8 H), 3.94 (s, 2 H), 0.92 (s, 36 H), 0.07 (s, 24 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 141.46, 140.89, 125.24, 121.49, 64.96, 41.88, 25.97, 18.42, –5.25 ppm. MS: m/z = 744.6 $[M]^+$. $C_{41}H_{76}O_4Si_4$ (745.39): calcd. C 66.07, H 10.28; found C 65.94, H 10.06.

One-Pot Cross-Coupling to Diarylmethanes: Acetophenone (3.1 mmol, 0.38 g) and bromobenzene (3.1 mmol, 0.49 g) and 1-bromo-4-methylbenzene (3.1 mmol, 1.06 g) or 1-bromo-4-fluorobenzene (3.1 mmol, 0.54 g) and 1-bromo-4-methylbenzene (3.1 mmol, 1.06 g) were used. After workup, the residue was subjected to column chromatography, and the product mixture was obtained as a colorless oil. For the product mixture of diphenylmethane, *p*-tolylphenylmethane, and di-*p*-tolylmethane: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.30 (m, 6.2 H), 7.18–7.22 (m, 8.6 H), 7.08 (s, 5.7 H), 3.98 (s, 1.6 H, CH_2 of diphenylmethane), 3.94 (s, 2 H, CH_2 of *p*-tolylphenylmethane), 3.89 (s, 0.4 H, CH_2 of di-*p*-tolylmethane), 2.38 (s, 1.1 H), 2.31 (s, 4.2 H) ppm. For the product mixture of bis(4-fluorophenyl)methane, 4-fluoro-4′-methyldiphenylmethane, and di-*p*-tolylmethane: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.04–7.13 (m, 14.2 H), 6.95–6.98 (t, J = 8.4 Hz, 5.9 H), 7.08 (s, 5.7 H), 3.94 [s, 0.3 H, CH_2 of bis(4-fluorophenyl)methane], 3.91 (s, 2 H, CH_2 of 4-fluoro-4′-methyldiphenylmethane), 3.89 (s, 2.48 H, CH_2 of di-*p*-tolylmethane), 2.31 (s, 1.98 H), 2.30 (s, 3.9 H) ppm.

4-Fluoro-4′-methoxydiphenylmethane:[7] Acetophenone (0.37 g, 3.1 mmol) and 1-bromo-4-methoxybenzene (0.58 g, 3.1 mmol) and 1-bromo-4-fluorobenzene (0.54 g, 3.1 mmol) were used. The product was obtained as a colorless oil (0.268 g, 40%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.10 (s, 2 H), 7.07 (d, J = 7.8 Hz, 2 H), 6.95 (t, J = 8.4 Hz, 2 H), 6.83 (d, J = 8.4 Hz, 2 H), 3.88 (s, 2 H), 3.76 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.53, 160.11, 158.01, 137.22, 133.02, 130.14, 130.06, 129.73, 127.99, 115.22, 115.01, 114.21, 113.90, 55.21, 40.14 ppm. MS: m/z = 216.2 $[M]^+$.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H NMR and ^{13}C NMR spectra for all synthesized compounds.

Acknowledgments

The authors gratefully acknowledge financial support from the National Natural Science Foundation of China (NSFC) (project numbers 21172087, 21172088, and 20972056) and in part from the self-determined research funds of the Central China Normal University (CCNU) from the colleges' basic research and operation of the Ministry of Education (MOE), China.

[1] a) K. Kurata, K. Taniguchii, K. Takashima, I. Hayashi, M. Suzuki, *Phytochemistry* **1997**, *45*, 485–487; b) H. H. Sun, V. J. Paul, W. Fenical, *Phytochemistry* **1983**, *22*, 743–745; c) L. Hari-

nantenaina, J. D. Bowman, P. J. Brodie, C. Slebodnick, M. W. Callmander, E. Rakotobe, R. Randrianaivo, V. E. Rasamison, A. Gorka, P. D. Roepe, M. B. Cassera, D. G. I. Kingston, *J. Nat. Prod.* **2013**, *76*, 388–393; d) X. Fan, N.-J. Xu, J.-G. Shi, *J. Nat. Prod.* **2003**, *66*, 455–458; e) M. Ma, J.-L. Zhao, S.-J. Wang, S. Li, Y.-C. Yang, J.-G. Shi, X. Fan, L. He, *J. Nat. Prod.* **2006**, *69*, 206–210; f) M. Ma, J.-L. Zhao, S.-J. Wang, S. Li, Y.-C. Yang, J.-G. Shi, X. Fan, L. He, *J. Nat. Prod.* **2007**, *70*, 337–341.

[2] a) M. Graffner-Nordberg, K. Kolmodin, J. Aqvist, S. F. Queener, A. Hallberg, *J. Med. Chem.* **2001**, *44*, 2391–2402; b) R. Silvestri, M. Artico, G. D. Martino, R. Ragno, S. Massa, R. Loddo, C. Murgioni, A. G. Loi, P. L. Colla, A. Pani, *J. Med. Chem.* **2002**, *45*, 1567–1576; c) R. A. Forsch, S. F. Queener, A. Rosowsky, *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1811–1815; d) G. Beaton, W. J. Moree, F. Jovic, T. Coon, J. Yu, *Sleep Inducing Compound and Methods Relating Thereto*. US2006/14797, **2006**; e) G. Panda, M. K. Parai, S. K. Das, Shagufta, M. Sinha, V. Chaturvedi, A. K. Srivastava, Y. S. Manju, A. N. Gaikwad, S. Sinha, *Eur. J. Med. Chem.* **2007**, *42*, 410–419; f) W. J. Moree, B.-F. Li, F. Jovic, T. Coon, J. Yu, R. S. Gross, F. Tucci, D. Marinkovic, S. Zamani-Kord, S. Malany, M. J. Bradbury, L. M. Hernandez, Z. O'Brien, J. Wen, H. Wang, S. R. J. Hoare, R. E. Petroski, A. Sacaan, A. Madan, P. D. Crowe, G. Beaton, *J. Med. Chem.* **2009**, *52*, 5307–5310; g) A. V. Cheltsov, M. Aoyagi, A. Aleshin, E. C.-W. Yu, T. Gilliland, D. Zhai, A. A. Bobkov, J. C. Reed, R. C. Liddington, R. Abagyan, *J. Med. Chem.* **2010**, *53*, 3899–3906; h) S. Messaoudi, A. Hamze, O. Provot, B. Tréguier, J. Rodrigo De Losada, J. Bignon, J.-M. Liu, J. Wdzieczak-Bakala, S. Thoret, J. Dubois, J.-D. Brion, M. Alami, *ChemMedChem* **2011**, *6*, 488–497.

[3] a) L. D. Hicks, J. K. Han, A. J. Fry, *Tetrahedron Lett.* **2000**, *41*, 7817–7820; b) S. Ogoshi, H. Nakashima, K. Shimonnaka, H. Kurosawa, *J. Am. Chem. Soc.* **2001**, *123*, 8626–8627; c) X.-J. Li, Y.-Y. Feng, L. Lin, G. Zou, *J. Org. Chem.* **2012**, *77*, 10991–10995; d) H. Yoshida, M. Watanabe, T. Morishita, J. Ohshita, A. Kunai, *Chem. Commun.* **2007**, *15*, 1505–1507; e) B. Hatano, D. Kubo, H. Tagaya, *Chem. Pharm. Bull.* **2006**, *54*, 1304–1307; f) T. Kobayashi, S. M. Rahman, *Synth. Commun.* **2003**, *33*, 3997–4003.

[4] a) A. García Martínez, J. O. Barcina, M. R. C. Heras, Á. F. Cerezo, *Org. Lett.* **2000**, *2*, 1377–1378; b) K. Itami, M. Mineno, T. Kamei, J.-I. Yoshida, *Org. Lett.* **2002**, *4*, 3635–3638; c) R. Kuwano, M. Yokogi, *Chem. Commun.* **2005**, *47*, 5899–5901; d) C. C. Kofink, P. Knochel, *Org. Lett.* **2006**, *8*, 4121–4124; e) H.-B. Sun, B. Li, S.-J. Chen, J. Li, R.-M. Hua, *Tetrahedron* **2007**, *63*, 10185–10188; f) B. Liégault, J.-L. Renaud, C. Bruneau, *Chem. Soc. Rev.* **2008**, *37*, 290–299; g) I. J. S. Fairlamb, P. Schnal, R. J. K. Taylor, *Synthesis* **2009**, *3*, 508–510; h) C. Duplais, A. Krasovskiy, A. Wattenberg, B. H. Lipshutz, *Chem. Commun.* **2010**, *46*, 562–564; i) N. Sakai, K. Kawana, R. Lkeda, Y. Nakaikc, T. Konakahara, *Eur. J. Org. Chem.* **2011**, 3178–3183; j) P. Maity, D. M. Shacklady-McAtee, G. P. A. Yap, E. R. Sirianni, M. P. Watson, *J. Am. Chem. Soc.* **2013**, *135*, 280–285; k) F. Zhao, Q. Tan, F.-H. Xiao, S.-F. Zhang, *Org. Lett.* **2013**, *15*, 1520–1523.

[5] a) S. P. Maddaford, B. A. Keay, *J. Org. Chem.* **1994**, *59*, 6501–6503; b) S. M. Nobre, A. L. Monteiro, *Tetrahedron Lett.* **2004**, *45*, 8225–8228; c) R. Kuwano, M. Yokogi, *Org. Lett.* **2005**, *7*, 945–947; d) G. A. Molander, M. D. Elia, *J. Org. Chem.* **2006**, *71*, 9198–9202; e) M. J. Burns, I. J. S. Fairlamb, A. R. Kapdi, P. Sehnal, R. J. K. Taylor, *Org. Lett.* **2007**, *9*, 5397–5400; f) X.-F. Wu, H. Neumann, M. Beller, *Adv. Synth. Catal.* **2011**, *5*, 788–792.

[6] J. R. Schmink, N. E. Leadbeater, *Org. Lett.* **2009**, *11*, 2575–2578.

[7] K. Endo, T. Ishioka, T. Ohkubo, T. Shibata, *J. Org. Chem.* **2012**, *77*, 7223–7231.

[8] a) B. C. Hamann, J. F. Hartwig, *J. Am. Chem. Soc.* **1997**, *119*, 12382–12383; b) D. A. Culkin, J. F. Hartwig, *J. Am. Chem. Soc.* **2001**, *123*, 5816–5817; c) L.-Q. Xue, Z.-Y. Lin, *Chem. Soc. Rev.* **2010**, *39*, 1692–1705; d) C.-S. Cao, L.-L. Wang, Z.-Y. Cai, L.-Q. Zahng, J. Guo, G.-S. Pang, Y.-H. Shi, *Eur. J. Org. Chem.* **2011**, 1570–1574.

[9] C. C. C. Johansson, T. J. Colacot, *Angew. Chem.* **2010**, *122*, 686–718; *Angew. Chem. Int. Ed.* **2010**, *49*, 676–707.

[10] F. Churruca, R. SanMartin, M. Carril, I. Tellitu, E. Domínguez, *Tetrahedron* **2004**, *60*, 2393–2408.

[11] a) X.-W. Hao, J. Yuan, G.-A. Yu, M.-Q. Qiu, N.-F. She, Y. Sun, C. Zhao, S.-L. Mao, J. Yin, S.-H. Liu, *J. Organomet. Chem.* **2012**, *706*, 99–105; b) L. Chen, G.-A. Yu, F. Li, X.-L. Zhu, B. Zhang, R. Guo, X.-Z. Li, Q.-H. Yang, S. Jin, C.-C. Liu, S.-H. Liu, *J. Organomet. Chem.* **2010**, *695*, 1768–1775.

[12] M. Palucki, S. L. Buchwald, *J. Am. Chem. Soc.* **1997**, *119*, 11108–11109.

[13] J.-D. Zhang, A. Bellomo, A. D. Creamer, S. D. Dreher, P. J. Walsh, *J. Am. Chem. Soc.* **2012**, *134*, 13765–13772.

[14] Y. Bonvin, E. Callens, I. Larrosa, D. A. Henderson, J. Oldham, A. J. Burton, A. G. M. Barrett, *Org. Lett.* **2005**, *7*, 4549–4552.

[15] F. Churruca, R. S. Martin, M. Carril, I. Tellitu, E. Domínguez, *Tetrahedron* **2004**, *60*, 2393–2408.

[16] T. Satoh, Y. Kawamura, M. Miura, M. Nomura, *Angew. Chem.* **1997**, *109*, 1820–1822; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1740–1742.

[17] C. He, S. Guo, L. Huang, A.-W. Lei, *J. Am. Chem. Soc.* **2010**, *132*, 8273–8275.

[18] A. Y. Lebedev, A. F. Asachenko, WO 2007/111537, **2007**.

Received: April 24, 2013
Published Online: ■

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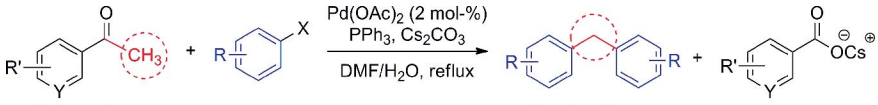
Palladium Catalysis



An aryl methyl ketone is used as the methylene donor to couple with two molecules of an aryl halide for the synthesis of various symmetric diarylmethanes under palladium catalysis. The mechanism involves a two-step coupling process in which the presence of a trace amount of H_2O is indispensable. The cross-coupling to unsymmetrical diarylmethanes with this method is also explored.

Keywords: Homogeneous catalysis / Palladium / Cross-coupling / C–C coupling / Reaction mechanisms

