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Aryl alkyl carbene-Pd complex assisted C-Cl bond activation: An unprecedented cross-coupling route to *trans*-stilbenes

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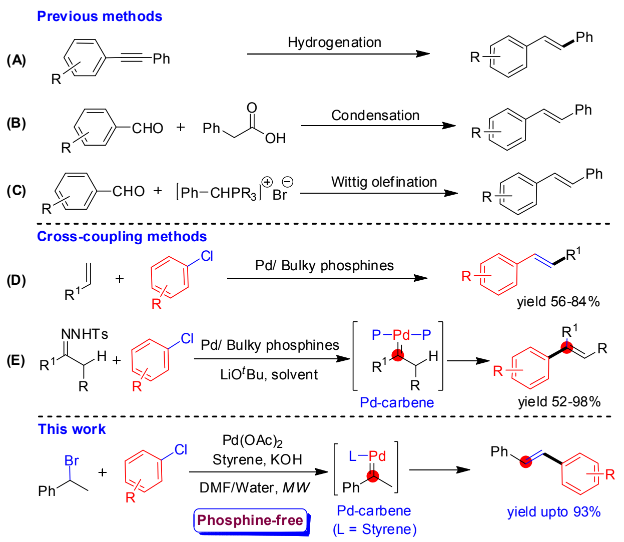
Palladium catalyzed cross-coupling with aryl chlorides has always been a challenge and does not take place without the assistance of bulky phosphine ligands, NHCs or other additives. In this work, we present an unprecedented phosphine-free coupling of cheap and less reactive substrates like aryl chlorides with 1-(bromoethyl)benzene as nucleophilic coupling partner at low Pd concentration, under microwave conditions to access highly regio- and stereospecific *trans*-stilbene derivatives. The reaction is believed to proceed *via* stable Pd-carbene intermediate generated *in-situ* under *MW* conditions from 1-(bromoethyl)benzene. Another key requirement in the reaction is the presence of styrene; as in its absence, Pd catalysed coupling of halogenated ethyl benzene with chloroarenes does not take place at all. DFT studies have also been carried out to get a thermodynamic insight into the proposed mechanism.

Introduction

Stilbene and oligostilbene derivatives which are frequently found in nature have become of particular interest owing to their wide range of biological activities including anticancer, antifungal, antioxidant, anti-HIV and anti-inflammatory.[1] The photochemical and photophysical properties of stilbene skeleton also make it suitable as a central chromophore for the production of dyes, pigments, fluorescent whitener, light emitting diodes, and organic based photo-voltaic solar cells.[2] Many synthetic routes to stilbene derivatives have been reported as shown in scheme 1. These include catalytic semi-hydrogenation of alkynes (Scheme 1A),[3] Aldol-type condensation of an aromatic aldehyde with phenylacetic acid (Scheme 1B),[4] from substituted benzaldehydes *via* Wittig or Horner–Wadsworth–Emmons reactions (Scheme 1C),[5] or *via* arylation of styrene derivatives (Heck reaction)[6] (Scheme 1D).

Since its discovery, the Mizoroki-Heck reaction which involves coupling of aryl iodides, bromides, triflates or diazonium salts with styrene in the presence of palladium catalyst and stoichiometric amount of base remains the best method for preparing stilbene derivatives.[7] While the method has been a subject of extensive research and taken up by chemical industry, the process economics remains a major concern.[8,9] It demands that the reaction should occur at low catalyst loadings whilst providing the product in high yield, follow a ligand-free protocol, and make use of readily available and cheap starting materials like organic chlorides instead of bromides and iodides. The limitation with chloroarenes, however, is that unlike aryl iodides and bromides, they are unreactive under the standard reaction conditions.[10] Catalytic systems especially designed for cross-coupling with aryl chlorides include air-sensitive, bulky and sometimes toxic phosphine ligands.[11-16] An additional problem encountered in stilbene synthesis *via* Heck coupling is that the coupling partners, styrenes have to be used in excess owing to a possible polymerization under usual high temperature conditions of the reaction.[17]



Scheme 1. Comparative illustration of previous work and this work

A solution to this problem has been offered in two former reports which demonstrate a Heck coupling by generating

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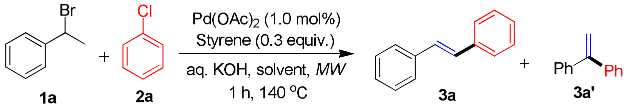
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

olefin from alkyl halides or alcohols *in-situ*.[18] While a dehydrohalogenative as well as a dehydrative Heck olefination with aryl iodides and bromides has been reported, its success with the less reactive and challenging aryl chlorides is less known.[19] In our efforts directed towards lifting these limitations and developing an economically useful C-C coupling involving a ligand-free C-Cl activation; we investigated the reaction of aryl chlorides with secondary alkyl bromides as coupling partners under microwave conditions. The reaction is believed to proceed *via* Pd-carbene complex yielding exclusively the β-arylated product. This is in contrast to the Pd-catalyzed cross-coupling of hydrazones with aryl halides (also involving a Pd-carbene complex) which affords the *α*-arylated product selectively (Scheme 1E).[20]

Results and Discussion

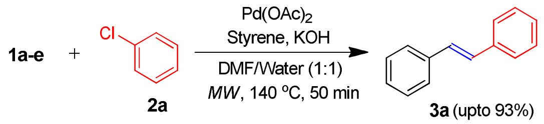
Our investigation started with the synthesis of 1-(bromoethyl)benzene (**1a**) by the reaction of styrene with hydrobromic acid in acetic acid. The product of hydrobromination containing **1a** and unreacted styrene approximately in the ratio 7:3 as determined by HPLC (Supporting Information Figure S1) was taken in DMF. To it, chlorobenzene (3.0 equiv.), followed by KOH (2.0 equiv.) in water was added. Finally, $Pd(OAc)_2$ (1.0 mol%) was added to the reaction mixture and it was irradiated in microwave for one hour at 140 °C. We were delighted to find that the desired product *trans*-stilbene (**3a**) was formed in 40% yield (Table 1, entry 2) along with unreacted **1a** and styrene while no traces of 1,1-diphenylethene (**3a'**) were seen (Scheme 2).[19] The product showed a singlet at 7.18 ppm in ^1H NMR for two olefinic protons indicating it to be a symmetrical alkene. Peaks in the aromatic region between 7.28-7.59 ppm for 10 protons confirmed the presence of two phenyl rings and λ_{max} at 296 nm in UV suggest it to be the *trans*- isomer of stilbene (Supporting Information Figure S2).

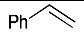
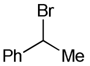
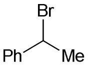
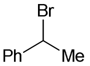
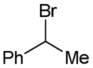
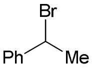
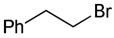
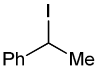
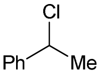
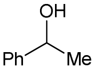


Scheme 2. Reaction of 1-(bromoethyl)benzene (**1a**) with chlorobenzene (**2a**)

In a surprising revelation, we discovered that when the same reaction was carried out with pure **1a** without any traces of styrene, the desired product **3a** was not formed at all (Table 1, entry 3). Also, interestingly as expected, another reaction with styrene as the starting substrate failed to yield stilbene under the employed reaction conditions, and was recovered as such (Table 1, entry 1) after the reaction. These observations were quite unique and important from the perspective of ligand-free C-C bond formation with aryl chlorides as coupling partners, and motivated us to explore the reaction in greater details. We were excited to find that lowering the Pd concentration from 1 mol% to 0.5 mol% and increasing KOH from 2.0 equiv. to 3.0 equiv. increased the yield of **3a** drastically from 40 to 93% (Table 1, entry 2 and 3). We surmised that the reason for an increased yield might be vested in particle size reduction of active Pd catalyst on lowering Pd concentration. With 0.5 mol% Pd loading, DLS demonstrated the existence of Pd-colloids with an average diameter of 17 nm (Supporting Information Figure S3). It is believed that low Pd concentrations suppress the formation of Pd-black keeping all the metal available for catalysis. Previously, *de* Vries and co-workers demonstrated a ligand-free Heck olefination of styrene with activated and unactivated aryl bromides and aryl iodides, using 0.05 mol% of $Pd(OAc)_2$ with NaOAc as base in NMP at 135 °C.[21] Their system, however failed completely with aryl chlorides as substrates. Through this work, however, we report for the first time a phosphine-free coupling of aryl chlorides with secondary alkyl bromide instead of styrene as coupling partner at low Pd loading. On changing the equivalents of styrene to 0.4 or 0.2, the yield of **3a** dropped to 60 and 70% respectively (Table 1, entry 4, 5) suggesting that 30% styrene in the reaction mixture was optimum for high product yield.

Table 1. Optimization of substrate for synthesis of *trans*-stilbene (3a)

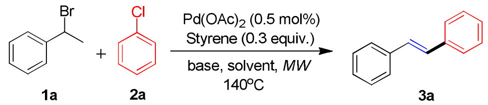


Entry[a]	Substrate	Styrene (equiv.)	$Pd(OAc)_2$ (mol%)	Yield (%; HPLC)
1		-	0.5	0
2	 **1a**	0.3	1.0	90, 40[b]
3	 **1a**	0.3	0.5	93, 0[c],0[d], 63[e]
4	 **1a**	0.4	0.5	60
5	 **1a**	0.2	0.5	70
6	 **1a**	0.3	0.25	66
7	 **1b**	0.3	0.5	80, 0[c]
8	 **1c**	0.3	0.5	67, 0[c]
9	 **1d**	0.3	0.5	45, 0[c]
10	 **1e**	0.3	0.5	33, 0[c]

[a] Reaction conditions: Substrate (**1a-e**) (1.0 equiv, 0.5 mmol), styrene, chlorobenzene (**2a**; 3.0 equiv; 2.0 mmol), KOH (3.0 equiv), $Pd(OAc)_2$, DMF:H_2O (1:1), MW, 140 °C, 50 min. [b] KOH (2.0 equiv); [c] No styrene added; [d] PPh_3 added in place of styrene; [e] $Pd(CH_3CN)_2Cl_2$ instead of $Pd(OAc)_2$.

To ascertain the role of styrene in the reaction, it was replaced by Ph_3P (Table 1, entry 3). However, under these conditions, compound **3a** was not formed at all suggesting that styrene as an additive was not facilitating the reaction simply by acting as a ligand, but had some hitherto unknown effect on kinetics of the reaction. Further, reactions of chlorobenzene with primary halide, 2-(bromoethyl)benzene (**1b**) under the same reaction conditions afforded **3a** in 80% yield (Table 1, entry 7). This prompted us to explore the effect of substrates in controlling coupling with chlorobenzene. For this, iodo- (**1c**), chloro- (**1d**) and hydroxyl (**1e**) analogues of **1a** were prepared.

Table 2. Optimization of substrate for synthesis of *trans*-stilbene (**3a**)



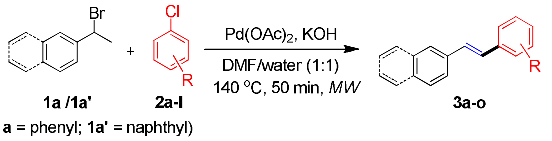
Entry	Solvent	Base	Yield (%;HPLC)	Time (min)
1	DMF	KOH	85	50
2	CH_3CN	KOH	0	50
3	H_2O	KOH	54	50
4	**DMF/H_2O**	**KOH**	**93,38[b],21[c]**	**50**
5	CH_3CN/H_2O	KOH	0	50
6	Acetone/H_2O	KOH	56	50
7	THF/H_2O	KOH	6	50
8	DMSO	KOH	0	50
9	DMSO/H_2O	KOH	0	50
10	DMF/H_2O	Et_3N	6	50
11	DMF/H_2O	K_2CO_3	66	50
12	DMF/H_2O	-	0	50
13	DMF/H_2O	[bmim]OH	48	50
14	DMF/H_2O	KOH	25[d]	50
15	DMF/H_2O	KOH	90[e]	50
16	DMF/H_2O	KOH	90	60
17	DMF/H_2O	KOH	63	40
18	DMF/H_2O	KOH	37, 0[f]	30

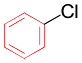
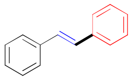
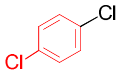
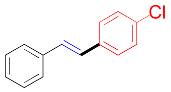
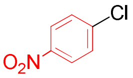
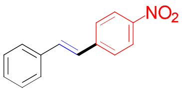
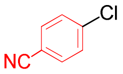
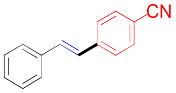
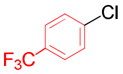
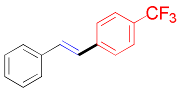
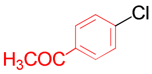
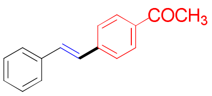
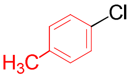
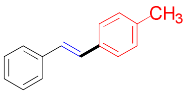
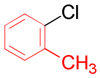
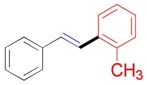
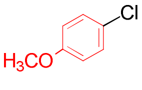
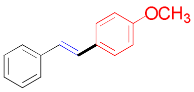
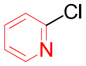
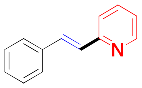
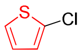
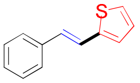
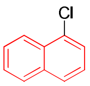
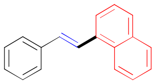
[a]Reaction conditions: 1-(bromoethyl)benzene, **1a** (1.0 equiv.), styrene (0.3 equiv.), chlorobenzene (3.0 equiv.), base (3.0 equiv.), Pd $(OAc)_2$ (0.5 mol%), MW, 140 °C, [b]KOH (2.0 equiv.), [c]chlorobenzene (2.0 equiv.), [d]reaction done at 120 °C, [e]reaction done at 160 °C, [f]conventional heating at 140 °C for 24 h.

As was seen with **1a**, in the absence of styrene, **3a** was not formed at all in all the three cases (Table 1; entry 8, 9, 10). While some unidentified polar impurities were obtained with **1c** and **1e**, the chloro- analogue (**1d**) was recovered as such after the reaction. However, on addition of 0.3 equivalent of styrene to (**1c-e**), **3a** was formed in 33-67% yields (Table 1; entry 8, 9, 10). All these results pointed out towards the fact that the reaction as anticipated early on did not follow a usual dehydrohalogenative Heck pathway involving an intermediate styrene. In fact, since all the substrates (**1a-e**) yielded **3a** as the major product, it indicated that all these reactions proceeded *via* a common intermediate which underwent facile coupling with chlorobenzene in contrast to previous reports where β-elimination mediated styrene formation was the preferred pathway.[18,19] Furthermore, it was apparent that presence of styrene (30 mol%) was inevitable for driving the reaction towards stilbene formation.

Since, the highest yield of coupled product **3a** was obtained from compound **1a**, further optimization to analyse the effect of solvent, temperature, time, amount of base, nature of base, and amount of chlorobenzene was carried out with **1a** as the substrate (Table 2).

Table 3 Scope of the reaction of **1a**/**1a'** with aryl and heteroaryl chlorides (**2a-l**)[a]



Entry[a]	Aryl halide (2)	Product (3)	Yield[b] (%)
1	 **2a**	 **3a**	86 (0)[c]
2	 **2b**	 **3b**	84
3	 **2c**	 **3c**	90
4	 **2d**	 **3d**	85
5	 **2e**	 **3e**	82
6	 **2f**	 **3f**	80
7	 **2g**	 **3g**	74
8	 **2h**	 **3h**	70
9	 **2i**	 **3i**	20
10	 **2j**	 **3j**	74
11	 **2k**	 **3k**	70
12	 **2l**	 **3l**	80

13	**2a**	**3m**	84[d]
14	**2k**	**3n**	74[d]
15	**2l**	**3o**	76[d]

[a]Reaction conditions: **1a** (1.0 equiv), aryl chloride (3.0 equiv), Pd(OAc)2 (0.005 equiv, 0.5 mol%), KOH (3.0 equiv), styrene (0.3 equiv), DMF/Water (1:1), 50 minutes under MW; [b]Isolated yield with respect to **1a**/**1a'**; [c]1.0 equiv of TEMPO was added; [d]Reaction was carried out with **1a'** (1.0 equiv) and vinyl naphthalene (0.3 equiv) in place of **1a** and styrene.

A series of polar solvents including DMF, CH_3CN, DMSO, water, DMF/H_2O, CH_3CN/H_2O, DMSO/H_2O, THF/H_2O and acetone/H_2O were screened. The results indicated that with 3.0 equivalent of KOH, highest yield of **3a** (93%) (Table 2, entry 4) was obtained in DMF/H_2O (1:1) in 50 minutes at 140 °C. On the contrary, in DMF and water alone as solvents, yield dropped to 85% and 54% respectively (Table 2, entry 1 and 3) owing to insolubility of base in one case and formation of a biphasic reaction mixture in the other. CH_3CN, DMSO and their aqueous solutions turned out to be poor choice of solvent and failed to yield any product (Table 2, entry 2, 5, 8, 9). Screening of various bases such as KOH, K_2CO_3, [bmim]OH, and triethyl amine showed that KOH worked best under the employed conditions (Table 2, entry 4, 10, 11, 13). Lowering the amount of KOH to 2.0 equivalents lowered the yield to 38% (Table 2, entry 4). Further, temperature variation in the range 120-160 ^{o}C demonstrated that 140 ^{o}C was ideal for the reaction. At 120 ^{o}C, reaction did not go to completion and **3a** was obtained in only 25% yield (Table 2, entry 14) while at 160 ^{o}C, yield was 90% which was almost the same as at 140 ^{o}C (Table 2, entry 15). Next, the reaction was monitored with respect to varied reaction times ranging from 30-60 minutes under *MW* irradiation and 24 hours under conventional heating. While the yield dropped significantly on decreasing the reaction time in *MW* (Table 2, entry 17, 18), to our astonishment, no trace of product was seen even after 24 hours under conventional heating. This observation emphatically highlighted the critical role of *MW* in producing an intermediate necessary for the progress of the reaction and its coupling with aryl chlorides. The best reaction conditions obtained after extensive optimization studies clearly demonstrated the high activity and efficiency of our catalytic system compared to any previous literature report on stilbene formation *via* cross-coupling with aryl chlorides.[22]

Under optimized conditions, we furthered our investigation into the scope of aryl chlorides as substrates for synthesis of substituted *trans*-stilbenes, and the results are summarized in Table 3. Both activated as well as inactivated aryl chlorides afforded moderate to high yield of products (70-90%), except for 4-chloromethoxy benzene (**2i**) which gave 1-methoxy-4-styrylbenzene (**3i**) in 20% yield. With chloro derivatives of pyridine (**2j**) and thiophene (**2k**), corresponding heterocyclic stilbene derivatives **3j** and **3k** were obtained in moderate yields. The generality of the reaction was further explored with 2-(1-bromoethyl)naphthalene (**1a'**) as the substrate. Under similar reaction conditions, substrate **1a'** after reaction with aryl chlorides afforded corresponding *trans*-olefins (**3m-o**) in moderate yields. All these studies clearly stated that for a phosphine-free C-C coupling of **1a** or **1a'** with chloroarenes at low Pd loading, 0.3 equivalent of styrene and *MW* conditions were indispensable.

Time dependent NMR

To get some insight into the mechanism, the reaction mixture was diagnosed at different times ranging from (0-50 min) through ^{1}H NMR spectroscopy (Figure 1 and 2). At the start of the reaction (0 min), the reaction mixture showed a doublet at 1.87 ppm (CH_3) and a quartet at 5.02 ppm (CH) arising from **1a**. The aromatic protons of compound **1a**, chlorobenzene and styrene appeared in the range of 7.02-7.40 ppm. Interestingly, it was observed that the quartet at 5.02 ppm disappeared after one minute, and two new quartets appeared upfield at 4.85 and 3.21 ppm. Further, the doublet at 1.87 ppm also vanished and was substituted by two new doublets at 1.47 and 1.34 ppm and a singlet at 2.1 ppm.

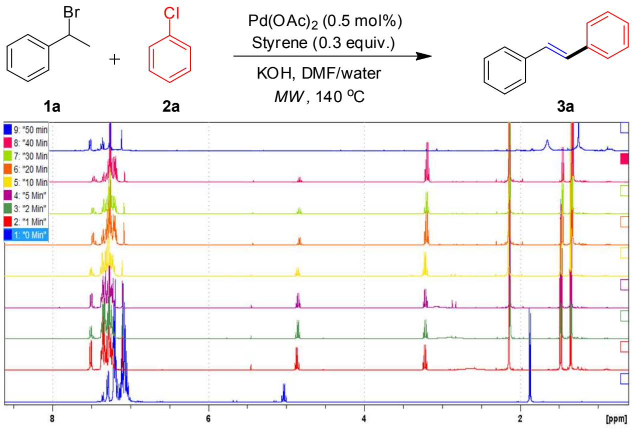


Figure 1. Time dependent 300 MHz ^{1}H NMR spectra showing progress of the reaction (0-50 min)

The emergence of these new signals pointed out towards formation of multiple species and intermediates in the reaction. The chemical shifts at 4.85(q) and 1.47(d) ppm were assigned to the CH and CH_3 protons of 1-(hydroxyethyl)benzene (**1e**) which might have formed from **1a** as a result of microwave assisted C-Br bond cleavage to yield benzyl radical (**I**) which upon attack from water in the medium afford **1e** as shown in Figure 3 (path I).

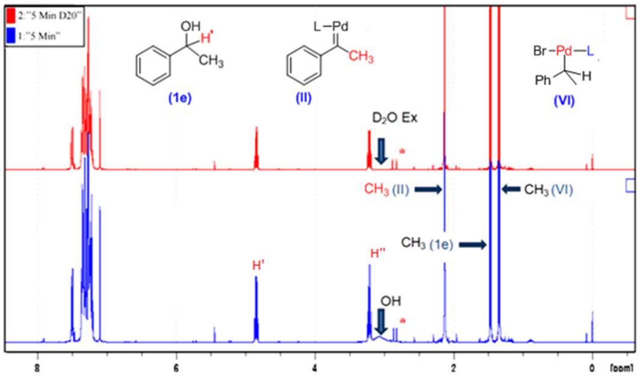


Figure 2. 300 MHz ^{1}H NMR spectrum of reaction mixture taken after 5 minutes. Lower spectrum (blue) in $CDCl_3$ and upper spectrum (red) showing D_2O exchange.

The disappearance of hydroxyl proton at 3.2 ppm on D_2O exchange confirmed the formation of **1e** during the reaction (Figure 2). Apparently, radical intermediate **I** undergo loss of hydrogen radical to yield a Pd-carbene complex (**II**) which is suggested by the methyl singlet at 2.12 ppm (Figure 2). The chemical shift at 3.21(q) ppm pointed out towards a significantly shielded benzylic proton which was originally at 5.02 ppm in **1a**. This shielding was contemplated to be a consequence of the coordination of benzylic carbon to Pd.

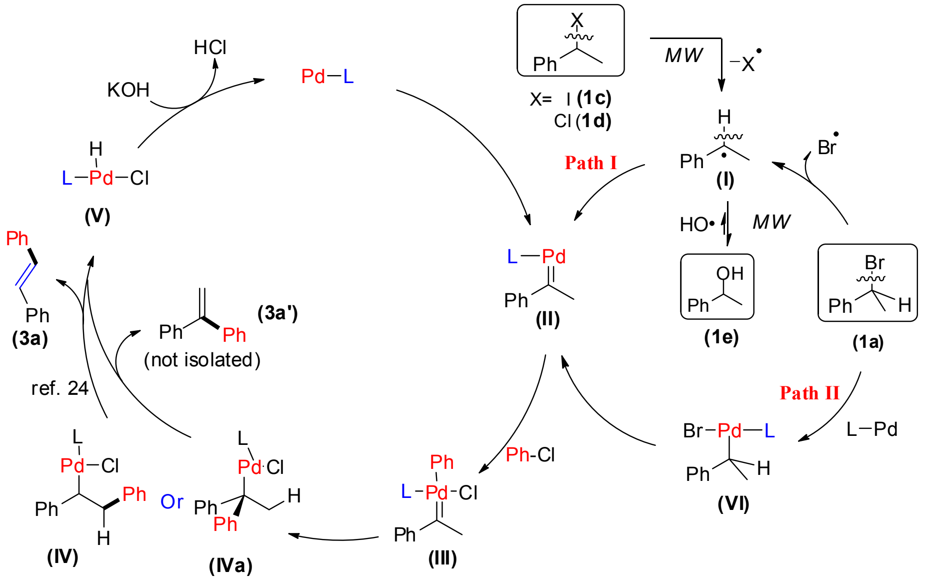


Figure 3. Plausible mechanism; (L = styrene)

It was envisaged that the reaction was also going through an alternate path of oxidative addition of **1a** to Pd(0) to yield intermediate **VI** which gave a doublet at 1.34 ppm and a quartet at 3.21 ppm in the ^{1}H NMR spectrum (Figure 1 and 2). Increasing the reaction time to 10 and 20 minutes did not bring about any noticeable change in the peaks of ^{1}H NMR spectra. The presence of multiple species that is 1-(hydroxyethyl)benzene (**1e**), Pd-carbene complex **II** and the oxidative addition intermediate **VI** was also evident from the ^{13}C NMR spectrum of the reaction mixture acquired at 10 min (see Supporting Information, spectrum 60). The benzylic carbon of **1e** and **VI** appeared at 70.1 and 66.0 ppm respectively consistent with the shielding behavior of the corresponding protons in the ^{1}H NMR spectra. Similarly, the methyl group in **1e**, **VI**, and **II** appeared at 25.3, 20.2, and 43.1 ppm respectively. Further, DEPT and COSY data at 10 min. supported the co-existence of these species in the reaction mixture (see Supporting Information Figure S4-6). LC-MS study of the reaction mixture at 1, 5, and 10 minutes showed evidence for the existence of Pd-carbene complex **II** (see Supporting Information Figure S7-9). The presence of Pd in the complex was also confirmed from EDAX spectra of the reaction mixture acquired after 5 minutes (see Supporting Information Figure S10). After 50 minutes, formation of *trans*-stilbene was evident from the disappearance of methyl singlet at 2.1 ppm and appearance of new peaks in the aromatic region. Further, x-ray[23] structure of compound **3c** confirmed the *trans*-geometry (Figure 4; see Supporting Information Figure S11 and Table S1 for details).

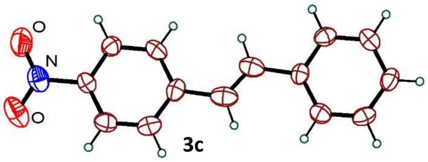


Figure 4. Single crystal X-ray molecular structure of compound **3c** showing *trans*-geometry

Mechanism

Guided by the spectroscopic data, we propose that the reaction is initiated *via* the homolytic C-Br bond cleavage facilitated under *MW* conditions. The evidence for radical initiated mechanism (path I) is supported by the fact that addition of 1.0 equivalent of TEMPO to the reaction mixture completely quenched the reaction with no trace of **3a** and more than 70% recovery of the starting substrate **1a** (Table 3). The bond cleavage is followed by two simultaneous protocols; first, the abstraction of hydrogen radical to yield a Pd-carbene complex (**II**) and subsequent attack by HO• to form the hydroxyl derivative **1e.** The C-Br bond cleavage appears to be quite facile as the entire **1a** is consumed within one minute of the reaction as can be seen in the ^{1}H NMR spectrum. The active Pd(0) catalyst is generated *in situ* from $Pd(OAc)_2$ in DMF-H_2O at high temperature. Another protocol which is believed to be going on in a parallel fashion is the oxidative addition of **1a** to Pd(0) to yield **VI** which on dehydrohalogenation yields the Pd-carbene monomer **II** stabilized by π-donor styrene ligand (Figure 3). The nucleophilicity of the Pd-carbene complex generated *in-situ* thereafter facilitates the oxidative addition of aryl chloride to yield intermediate **III,** followed by preferential 1,3-migration[24] of aryl group to yield intermediate **IV**. This is followed by β-elimination to yield the corresponding *trans*-stilbene (**3a**) and then reductive elimination of Pd(II) (**V**) to regenerate the active Pd(0) species.[25]

DFT studies

Further, to support our mechanistic pathway as shown in figure 3, DFT[26] studies with GAUSSIAN09 program[27] were performed. The structure of the molecules was optimized at the hybrid Becke3LYP (B3LYP) level in in *N*,*N*-dimethylformamide-water binary solvent *via* direct inversion in iterative subspace (DIIS), until the largest component of the ionic forces attained a value 0.00045 a.u. The B3LYP method can effectively be used in theoretical investigations of these type of reactions.[28d-h] The 6-311++G (2d,p) basis set[26] was chosen to describe H, C, O, Cl, and Br atoms and the effective core potential of Hay and Wadt[29] with double-ζ valence basis set (LANL2DZ) was used for the palladium (Pd). Absence of imaginary vibration during harmonic vibration frequency calculations confirmed that the optimized structures are at the local minima. The polarisable continuum model (PCM) using the integral equation formalism variant (IEFPCM)[30] was employed to investigate the effect of the solvent. The solvent descriptors were assumed to vary linearly with the molar fraction of each component of the homogeneous mixture. The free energy of the optimized structures in binary solvent is given in Table S3 of the supplementary data. The typical substrate **1a** and chlorobenzene **2a** was used as the model for calculation. The relative free energies ($G°_{rel}$) were computed, based on stoichiometric considerations. The free energy of the starting material 1-bromoethyl benzene **1a** was arbitrarily taken as zero and the relative free energy of other intermediate molecules and complexes was normalized to **1a**.

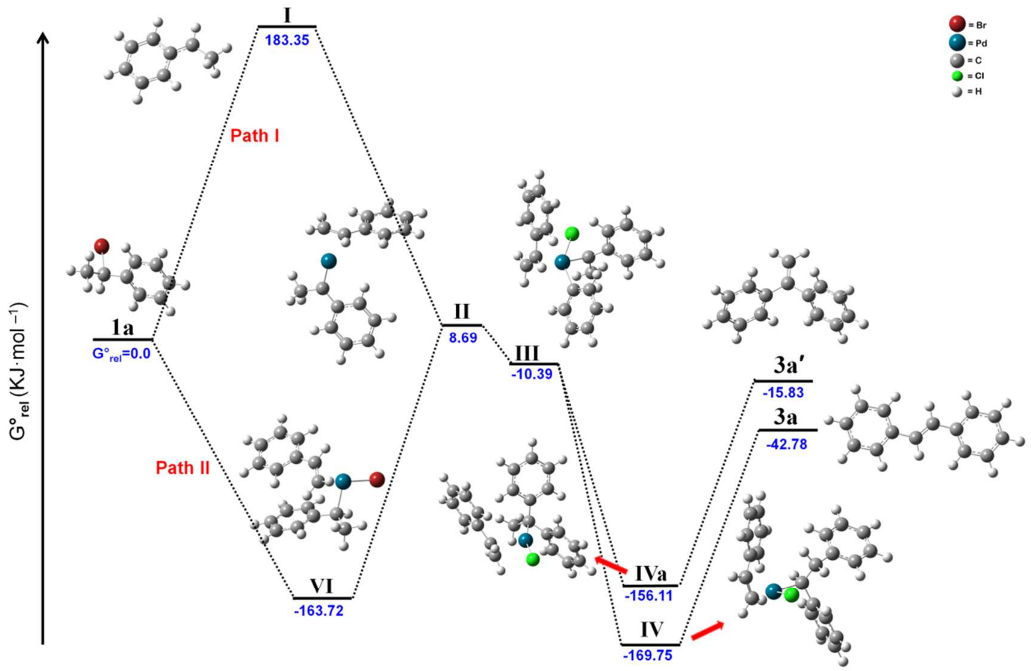


Figure 5. Potential Energy Surface of mechanistic pathway postulated in figure 3. Relative Gibbs Free Energy ($G°_{rel}$) given in kJmole^{-1}. $G°_{rel}$ calculated w.r.t. 1-(bromoethyl)benzene **1a** ($G°_{1a}$ = 0.0) in binary solvent DMF-H_2O. For structure clarification, see Supporting Information Table S2-19.

The proposed mechanism as shown in figure 3, supported largely by the NMR and mass spectral evidences was verified further by DFT studies (Figure 5). The aim was to identify intermediates which are thermodynamically stable and to compute free energy of overall reaction. In a way, we attempted to provide conformity to the formation of the species contemplated on the basis of the NMR spectra. The catalytic cycle starts with oxidative addition of Pd(0) to compound **1a** to yield an intermediate **VI** which is predicted to be quite stable. The relative free energy (G°_{rel}) of intermediate **VI** in binary solvent is -163.72 kJ mol^{-1}. This is also justified by its appearance and existence till 40 minutes in the ^{1}H NMR spectrum (1-40 min.). Dehydrohalogenation of **VI** yields the Pd-carbene monomer **II** (G°_{rel} = 8.69 kJ mol^{-1}). Complexation with π-donor ligands like styrene/vinyl naphthalene is predicted to provide the resting state (transient intermediate) to the Pd-carbene (see supporting information Figure S12). Similar formation of ligand stabilized Pd-carbene complexes is already known in literature[19] and has also been theoretically verified by DFT calculations.[19d] The G°_{rel} of ligand stabilized Pd-carbene complex predicts that in the presence of one ligand, the electrosteric stabilization is maximum. At the B3LYP level of theory, Pd-carbene when attached to one ligand has a lower relative free energy than with two ligands (see supporting information Figure S12). These transient intermediates are expected to promote C-Cl bond activation in chloroarenes resulting in the formation of intermediate **III** (G°_{rel} = -10.39 kJ mol^{-1}). Aryl migration in **III** can lead to either **IV** (G°_{rel} = -169.75 kJ mol^{-1}) or **IVa** (G°_{rel} = -156.11 kJ mol^{-1}). Because of less steric hindrance, complex **IV** shows greater stability than **IVa** by 13.64 kJ mol^{-1}. This is in agreement with the experimentally isolated product, *trans*-stilbene (**3a**) obtained from β-elimination of **IV** in contrast to 1,1-diphenyl ethane (**3a'**) which was not isolated. The free energy of the overall reaction is -42. 78 kJ mol^{-1}.

Conclusions

In this work, we demonstrate an unprecedented Pd catalysed cross-coupling reaction that employs secondary alkyl bromides as nucleophilic coupling partners. The protocol offers a phosphine-free C-Cl activation pathway facilitated by styrene stabilized Pd-carbene complex **II** generated *in-situ* under microwave conditions. The main features of this new methodology are: (i) it allows the use of aryl chlorides as inexpensive coupling partners; (ii) no need for expensive phosphine ligands; (iii) works with Pd loading as low as 0.5 mol%; (iv) secondary alkyl bromides as nucleophilic coupling partners instead of styrene used in *trans*-stilbene synthesis *via* Heck reaction; (v) diaryl and heteroaryl olefins can be prepared with high regio- and stereoselectivity and functional group tolerance; (vi) generation of aryl alkyl-carbene from 1-(bromoethyl)benzene as precursor under *MW* conditions; (vii) for the first time we demonstrate the styrene stabilized Pd-carbene complex in promoting C-Cl bond activation, a process that has previously been reported only with *N*-heterocyclic carbenes. We have also theoretically verified the mechanism by DFT studies which has provided us with a thermodynamic justification to the formation of the proposed reaction intermediates. For these reasons, we believe that the current methodology holds promise as an economically viable cross-coupling protocol with easy scale up. Future work will include detailed mechanistic investigation into determining the exact role of styrene *via* kinetic tests and extension of this concept to other transition metals.

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Notes and references

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‡ Electronic Supplementary Information (ESI) available: Detailed experimental procedures, copies of ^{1}H NMR, ^{13}C NMR and mass spectra for all the new compounds, X-ray crystallographic data for **3c**, and computational data related to the optimized geometry of intermediates and transition states. HPLC, UV-Vis, EDAX and LC-MS data available.

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