

A Novel Electromagnetic Mill Promoted Mechanochemical Solid-State Suzuki–Miyaura Cross-Coupling Reactions: Ultra-Low Catalyst Loading without Molecular Dispersants

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Abstract

The Nobel-prize-winning Suzuki-Miyaura cross-coupling(SMC) is a practical and attractive strategy for the construction of C-C bonds in both academic and industrial settings. However, the development of solid-state SMC reactions remains extremely scarce. Herein, we report the first electromagnetic mill(EMM) promoted solid-state SMC reaction using ultra-low palladium loading(0.05 mol%) without any molecular dispersants. This protocol exhibits substantially broadened substrate scope, good functional groups tolerance and efficient gram-scale synthesis, especially, provides relative high yields. The utility of this strategy was exemplified in the modification of photoluminescence molecules, cross-coupling of slightly soluble compound and synthesis of several important bioactive molecules. Furthermore, the XPS analyses on the oxidation state changes of palladium catalyst suggest the involvement of Pd^I intermediate which might be the active catalytic species. This solvent-free solid-state EMM-SMC was potential developed into industrially attractive and environmentally friendly routes, and the EMM system developed in this study could unlock broad areas of chemical space for solvent-free solid-state metal-catalyzed syntheses of valuable targets in various scientific fields.

Main Text

Historically, most of the organic transformations adopt solution-based methods, in which solvent are essential to dissolve the reactants and catalysts. More generally, solvent waste in the pharmaceutical industry and fine chemicals industry led to a formidable challenge for the sustainability of chemical synthesis;^{1,2} because an estimated 85% of waste by mass is attributable to organic solvent used in any organic reactions.³⁻⁶ Most organic solvents are toxic and easy to catch fire or explode, resulting in huge security risks in the production process. Notably, solvent recycling system have been well established to reduce solvent waste effectively, however, it is still wasteful of fossil-derived materials, environmentally problematic, hazardous and energy-demanding with regard to solvent production, purification and recycling⁷. Therefore, it is extremely desirable to develop green and sustainable synthetic technique.

The best solution for the solvent issue is to avoid using any harmful organic solvent. Therefore, solid-state organic reactions have attracted considerable interest in a variety of research areas as cleaner and sustainable synthetic alternatives^{4-6,8-11}. Furthermore, solid-state reactions are particularly suitable for the poorly soluble substrates in common organic solvents^{8,11-13}. However, the organic molecules are arranged tightly and regularly, leading to poor mixing efficiency of the reactants and/or catalysts. Thus, to develop highly efficient solid-state organic transformation is of great interest in synthetic chemistry and still remains challenging.

'Mechanochemistry' refers to transformations, normally of solids, induced by mechanical energy, such as by grinding, milling, pulling, shearing and sonication¹⁴. Since Ostwald proposed the term mechanochemistry in 1887, mechanochemical synthesis has been extensively investigated in polymer chemistry¹⁵, materials science^{16,17} and inorganic synthesis¹⁸. However, the application of

mechanochemistry to organic transformations is more recent¹⁹⁻⁴¹. So far, most of the examples are focusing on grinding or milling, and the process might promote the reactivity by ensuring thorough mixing and agitation of reactants, particle comminution down to nanometer sizes and creation of activated (amorphous) high-energy phases or zones of high temperature and pressure, which could not be reached in conventional stirring^{42,43}.

The Nobel-prize-winning Suzuki–Miyaura cross-coupling(SMC) is a practical and attractive strategy for the construction of C-C bonds in both academic and industrial settings⁴⁴⁻⁴⁷. More than 60% of the C-C bond is constructed via SMC in medicinal chemistry⁴⁸. Importantly, the classic asymmetric biaryl compounds constructed via SMC are an extensive structural scaffold in pharmaceuticals^{45,49-52}. Conventionally, SMC reactions are performed in organic solvents, however, the solvent free reactions, especially for solid-state couplings, have remained extremely scarce. So far, the limited number of mechanochemical conditions are using ball milling^{19,22,25,53-58} (Figure 1A). Since 2000, some progresses in solvent-free SMC reactions were reported, and various additives were applied to inhibit aggregation of the catalysts and substrate, such as NaCl, AgNO₃, methanol, H₂O, TEA, Al₂O₃, chitosan and so on,^{54-57,59-61} however, the homocoupling issue and limited substrates scope were still needed to figure out.

In addition, the scope of substrates is significantly restricted to electrondeficient aryl halides with low conversion rates. Furthermore, liquid-assisted grinding (LAG) by using a small amount of solvent, has emerged as a common strategy for solid-state reactions. Notably, Ito group demonstrated an olefin-accelerated solid-state SMC reaction using ball milling in 2019 (Figure 1B-1)⁶². They find that olefin additives could act as efficient molecular dispersants to inhibit the deleterious aggregation of palladium catalyst in solid state reactions⁶³. Very recently, Ito et. al provide an extremely fast and highly efficient method for cross-coupling reactions of insoluble aryl halides with large polyaromatic structures via a high-temperature ball-milling technique(Figure 1B-2)⁶⁴. Both 1,5-cod and H₂O play important roles in this transformations. However, it is still challenging to realize solvent free strategies for solid-state organic reactions avoiding any liquid additives due to the poor mixing efficiency and deleterious aggregation of reactants and/or catalysts. Thus we sought to design a new concept to solve this issue in solid-state SMC.

The electromagnetic mill(EMM) is a novel grinding device, using small ferromagnetic particles as the grinding media in a rotating electromagnetic field⁶⁵. The basic elements of the EMM are inductor of rotating magnetic field and placed in its axis tube, serving as a working chamber. Unlike the conventional ball mills, the mill housing is stationary while the grinding takes place in the working chamber using some small ferromagnetic rods to move as grinding media. The movement of ferromagnetic rods is caused by the action of the vortex electromagnetic field. The effectiveness and efficiency of the EMM process is dependent on the size parameters of the rods and the speed and intensity of the rotating electromagnetic field. So far, the EMM is only utilized in shredding of the raw material and ultra-fine comminution.⁶⁸⁻⁷¹

Considering on the issue of low reaction efficiency due to aggregation in solid state, we design and develop a new EMM equipment for solid-state coupling reactions, which might potentially solve this problem. Herein, we report the first EMM promoted solid-state SMC reaction using ultra-low catalyst loading without molecular dispersants (Figure 1B-3).

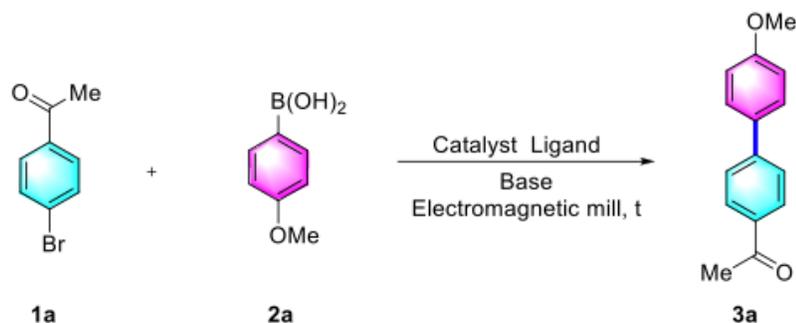
We initially conducted a study to optimize the EMM promoted SMC (EMM-SMC) reaction using 1-(4-bromophenyl)ethan-1-one(1a) and (4-methoxyphenyl)boronic acid(2a). Reactions were conducted in a electromagnetic mill in a flat bottom flask (10 mL) (or in a stainless-steel milling jar as shown in Fig. 1C) at 50 Hz using ferromagnetic rods (diameter: 0.35 mm, long: 5 mm). First of all, we focused on a high-performance Pd(OAc)₂/DavePhos catalyst system that has been reported by Ito and co-workers using ball milling¹⁷, notably, without any liquid-assisted grinding (LAG), 1-(4'-methoxy-[1,1'-biphenyl]-4-yl)ethan-1-one (3a) was obtained in 82% within 3 hour (Entry 1, Table 1). The highly catalytic efficiency inspired us to decrease the catalyst loading, interestingly, the yield of 3a was increased to 93% with 0.5 mol% Pd(OAc)₂ loading. Further to decrease the loading amount of Pd(OAc)₂ to 0.1 mol% and 0.05 mol%, the coupling product was obtained in 95% (Entries 2-3). However, the yields decreased sharply with 0.02 mol% or 0.01 mol% loading of Pd(OAc)₂. Subsequently, bases such as K₂CO₃, Cs₂CO₃, KOAc and KF, were investigated and KF could improve the yield to 97% (Entries 7-10). Next, a variety of ligands were examined, however, no better yields was obtained (Entries 11-17). Furthermore, we attempted different catalysts such as PdCl₂, Pd(dppf)Cl₂, Pd₂(dba)₃, Pd(dba)₂ and PdCl₂(MeCN)₂ (Entries 18-22), delightfully, the corresponding products 3a was formed in quantitative yields when PdCl₂(dppf) was utilized and the reaction time was shorted to 1 hour (99%, entry 19).

To explore the scope of the solid-state SMC reaction, a variety of solid aryl halides and arylboronic acid was investigated (Table 2). The reaction of 1-(4-bromophenyl)ethan-1-one(1a) with *o*-methoxyboronic acid (2b) proceeded to provide the desired coupling product 3b in 92% yield which is slightly lower than with *p*-methoxyboronic acid (2a). Both unsubstituted (2c) or alkyl substituted arylboronic acid (*o*-Me: 2d, *p*-tBu: 2e, 2,4,6-tri-methyl: 2f) were coupled in high yields under the optimized conditions (3c-3f). Arylboronic acid containing OCF₃ group also provided the corresponding products in 85% yield (3g). The developed conditions were also applied to the arylboronic acid bearing halides (2-F, 2-Cl, 4-F, 2,4-di-F, 3,4-di-Cl, 3,5-di-F and 3,5-di-Cl), which afforded the desired products in good to high yields (3h-3n: 71%-91%). Arylboronic acid with strong electron-withdrawing group worked very well to deliver the coupling molecule in both 79% (3o and 3p). Furthermore, other aromatic cores such as coumarone (2q), oxydibenzene (2r), and naphthalene (2s and 2t), efficiently formed the corresponding products in 73%-91% (3q-3t). The coupling of 4-bromobenzonitrile with boronic acid bearing 1-phenylnaphthalene (2u) 4-phenylmorpholine (2v) and (4-propylcyclohexyl)benzene, performed very well to afford the desired molecules in moderate to good yields (3u-3w). Notably, the introduction of 1,1':3',1''-terphenyl also worked smoothly to deliver 3x in 67% yield.

Subsequently, we turned our attention to the scope of aryl bromides (Table 2b). Simple aryl bromides bearing electron-withdrawing groups such as cyano, aldehyde, nitro, carbonyl and chloro groups provided

the desired products (4a-4e) in good to high yield (64%–92%). The strong electron-donating group substituted aryl bromides such as 2-bromo-4,6-dimethylaniline and 4-bromo-N,N-dimethylaniline proceeded smoothly to furnish the coupling products 4f and 4g in 75% and 72% respectively. The *p*-terphenyl and 2-phenylnaphthalene derivatives 4h and 4i were obtained efficiently under the standard conditions (82% and 93%). (4-Bromophenyl)(phenyl)methanone and 5-bromo-2,3-dihydro-1H-inden-1-one coupled with *p*-bromoacetophenone to afford 4j and 4k in high yields (84% and 85%). In addition, aryl bromides bearing thiophene, dibenzothiophene, 2-acetylpyridine or indole motif (Core of various intermediates for drugs and OLED), produced the corresponding products in moderate to high yields (4l-4p). Then the introduction of multi-aromatic scaffold to boronic acid could also proceed efficiently to produce the corresponding compounds in 62%-81% yield (4q-4t). Furthermore, some aryl iodides were also investigated which delivered the corresponding products in good yields (5a-5c). Especially, the unprotected phenol could survive very well under the standard conditions (5a-5b).

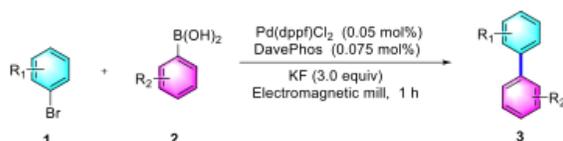
Table 1. Optimization Study on the EMM Promoted SMC Reaction.



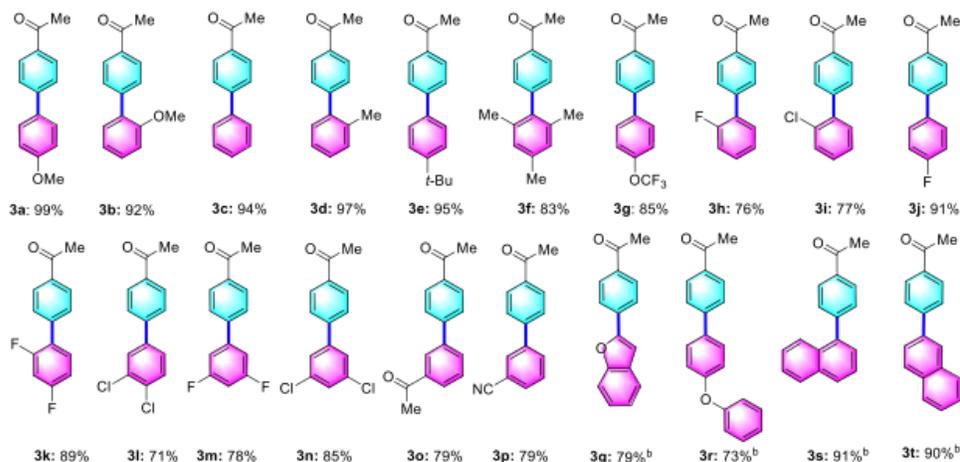
Entry	Catalyst	Ligand	Base	time/h	Yield/% ^b
1	Pd(OAc) ₂ (3 mol%)	DavePhos	CsF	3	82
2	Pd(OAc) ₂ (0.5 mol%)	DavePhos	CsF	3	93
3	Pd(OAc) ₂ (0.1 mol%)	DavePhos	CsF	3	95
4	Pd(OAc) ₂ (0.05 mol%)	DavePhos	CsF	3	95
5	Pd(OAc) ₂ (0.02 mol%)	DavePhos	CsF	3	56
6	Pd(OAc) ₂ (0.01 mol%)	DavePhos	CsF	3	32
7	Pd(OAc) ₂ (0.05 mol%)	DavePhos	K ₂ CO ₃	3	76
8	Pd(OAc) ₂ (0.05 mol%)	DavePhos	KOAc	3	73
9	Pd(OAc) ₂ (0.05 mol%)	DavePhos	Cs ₂ CO ₃	3	50
10	Pd(OAc) ₂ (0.05 mol%)	DavePhos	KF	3	97
11	Pd(OAc) ₂ (0.05 mol%)	dppf	KF	3	86
12	Pd(OAc) ₂ (0.05 mol%)	xphos	KF	4	84
13	Pd(OAc) ₂ (0.05 mol%)	PCy ₃	KF	5	73
14	Pd(OAc) ₂ (0.05 mol%)	PPh ₃	KF	5	88
15	Pd(OAc) ₂ (0.05 mol%)	PhDavePhos	KF	3	81
16	Pd(OAc) ₂ (0.05 mol%)	Ruphos	KF	3	82
17	Pd(OAc) ₂ (0.05 mol%)	1,1'-Bis(diisopropylphosphino)ferrocene	KF	3	79
18	PdCl ₂ (0.05 mol%)	DavePhos	KF	1	79
19	Pd(dppf)Cl₂ (0.05 mol%)	DavePhos	KF	1	99
20	Pd ₂ (dba) ₃ (0.05 mol%)	DavePhos	KF	3	79
21	Pd(dba) ₂ (0.05 mol%)	DavePhos	KF	3	56
22	PdCl ₂ (MeCN) ₂ (0.05 mol%)	DavePhos	KF	1	90
23	Pd(dppf)Cl ₂ (0.05 mol%)	-	KF	1	85

^a Conditions: 1 (1.0 mmol), 2 (1.2 mmol), [Pd]/ligand (1:1.5), base (3.0 mmol), in a flat bottom flask (10 mL) with ferromagnetic rods (5 g), EMM 50 Hz. ^b Isolated yields

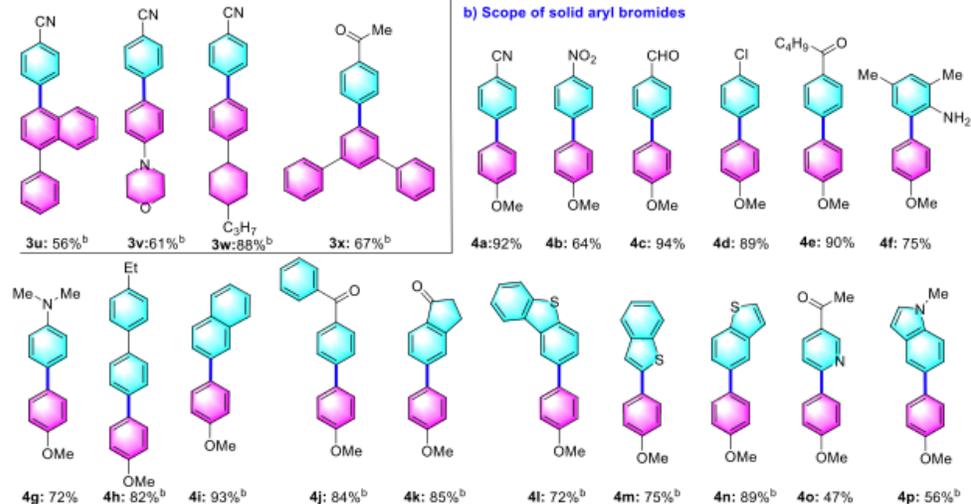
Table 2. Substrate Scope of Solid-State EMM-SMC Reaction.^{a,c}



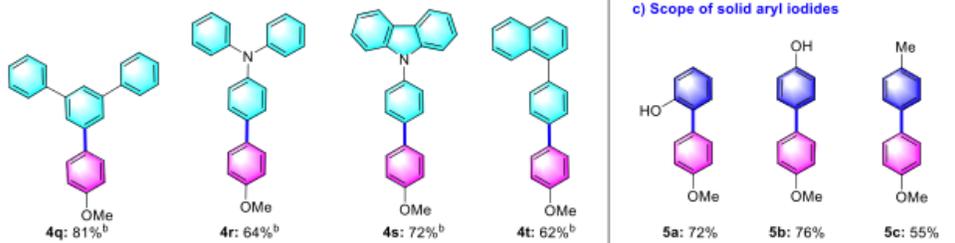
a) Scope of solid boronic acids



b) Scope of solid aryl bromides

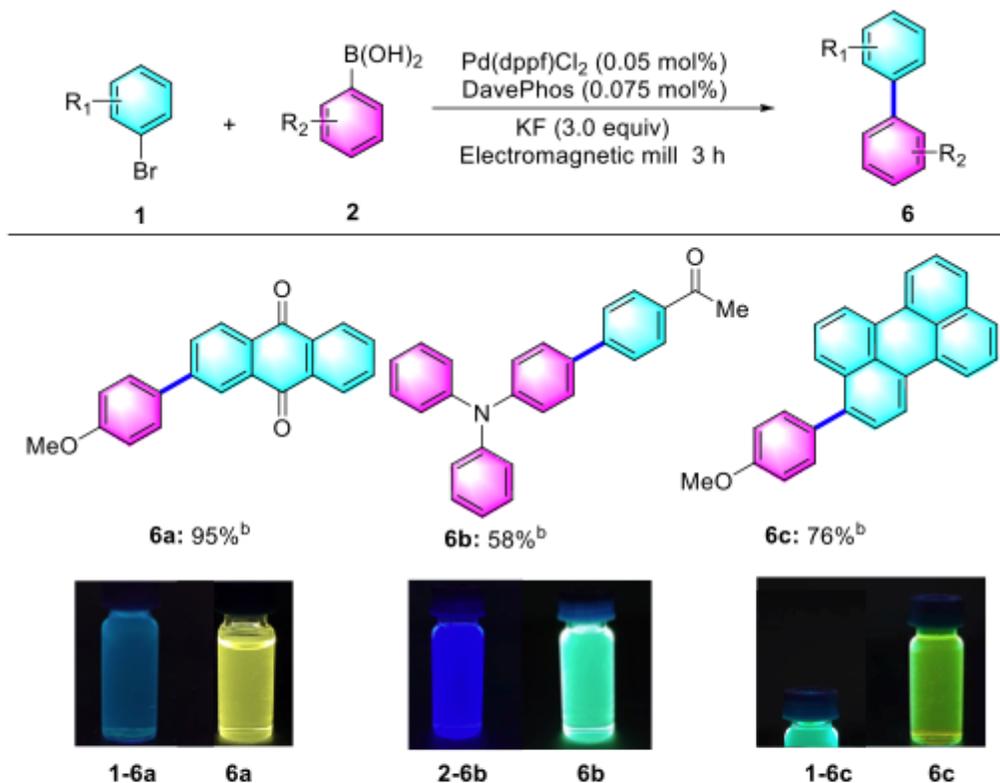


c) Scope of solid aryl iodides



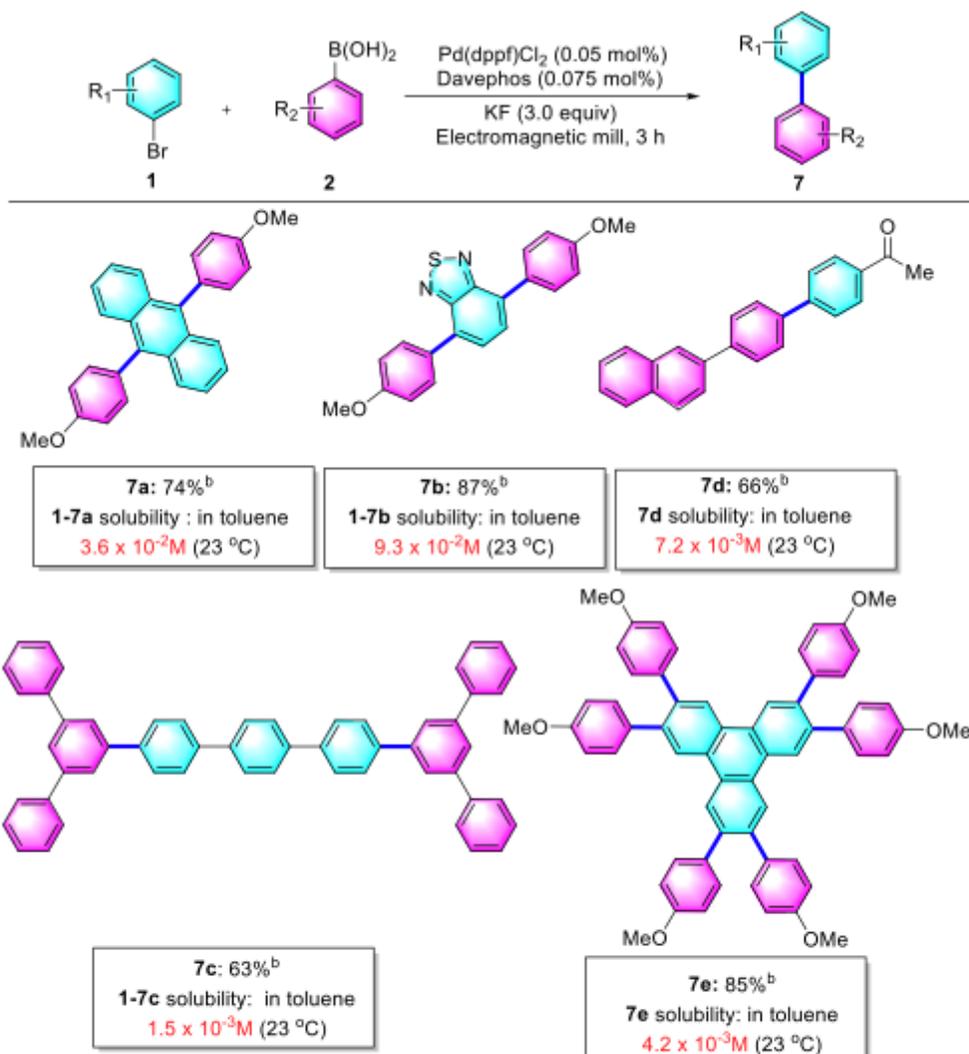
^a Conditions: 1 (1.0 mmol), 2 (1.2 mmol), Pd(dppf)Cl₂ (0.0005 mmol), DavePhos (0.00075 mmol), KF (3.0 mmol), in a flat bottom flask (10 mL) with ferromagnetic rods (5 g), EMM 50 Hz, 1 h. ^b Reaction time: 3 h. ^c Isolated yield.

Table 3. The Modification of Photoluminescence Molecules *via* EMM-SMC.^a



^aIsolated yield. ^b Conditions: 1-6 (1.0 mmol), 2-6 (1.2 mmol), Pd(dppf)Cl₂ (0.0005 mmol), DavePhos (0.00075 mmol), KF(3.0 mmol), in a flat bottom flask (10 mL) with ferromagnetic rods (5 g), 50 Hz, 3 h.

Table 4. Solid-State SMC Reactions of Slightly Soluble Compound.^a



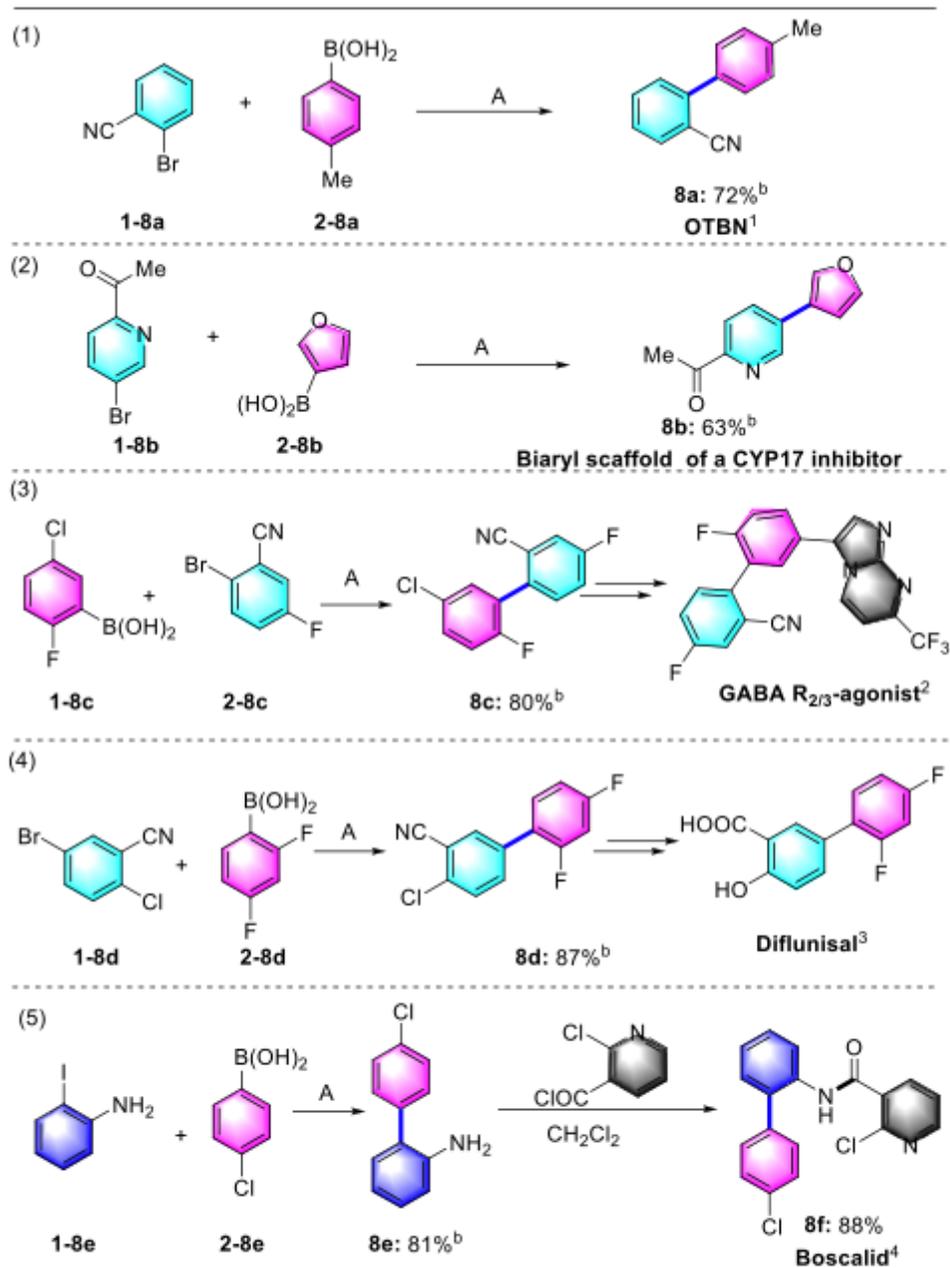
^aIsolated yield. ^b Conditions: **1-7** (1.0 mmol), **2-7** (1.2 mmol), Pd(dppf)Cl₂ (0.0005 mmol), DavePhos (0.00075 mmol), KF (3.0 mmol), in a flat bottom flask (10 mL) with ferromagnetic rods (5 g), EMM, 50 Hz, 3 h.

To further investigate the functional group compatibility and practicality of the developed EMM-SMC, it was used to the modification of photoluminescence molecules. The scaffolds of photoluminescence molecules bearing anthracene-9,10-dione, triphenylamine, dibenzopyrrole or perylene worked smoothly to generate the corresponding molecules in good to excellent yields (**6a**: 95%, **6b**: 58% and **6c**: 76%) (Table 3). As shown at the bottom of table 3, the fluorescence of the core scaffolds could be regulated efficiently *via* EMM-SMC reaction, such as introducing anisole group to anthracene-9,10-dione **1-6a** could change the fluorescence from light blue to yellow (**6a**), acetophenone regulated the fluorescence of triphenylamine from blue to light green (**6b**) and the installation of anisole to perylene could induce strong yellowish-green emission (**6c**) (in chloroform).

Subsequently, the EMM-SMC reaction was applied in the synthesis with solubility issues. Aryl halides with a solubility of 10^{-2} – 10^{-3} M, designated “slightly soluble” in the U.S. Pharmacopoeia⁷² often require a large amount of solvent in homogeneous solution based reactions, leading to the cross-coupling very

slow and inefficient. To our delight, the transformation of the insoluble aryl halides could proceed efficiently under EMM conditions without neither molecular dispersant nor heating, delivering the corresponding products in good yields (7a: 74%, 7b:87%, 7c: 63%). On the other hand, the target molecules with poor solubility could also be furnished under the standard conditions, providing 7d in 66% and 7e in 85% yields.

Table 5. Synthesis of Bioactive Molecules *via* EMM-SMC.^a



^aIsolated yield. ^bConditions A: 1-8(1.0 mmol), 2-8(1.2 mmol), Pd(dppf)Cl₂ (0.0005 mmol), DavePhos (0.00075 mmol), KF (3.0 mmol), in a flat bottom flask (10 mL) with ferromagnetic rods (5 g), EMM, 50 Hz, 3 h.

Furthermore, we examined the EMM-SMC reaction in the synthesis of bioactive molecules. The *o*-tolyl benzonitrile (OTBN) utilized in the synthesis of six different sartan-class drugs for the treatment of hypertension, could be efficiently achieved *via* EMM-SMC reaction of 2-bromobenzonitrile with *p*-tolylboronic acid (8a: 72%) (Eq 1, Table 5).⁷³ A furan-containing pharmaceutical intermediates 8b (CYP17 inhibitor) were successfully prepared in 63% yield (Eq 2, Table 5).⁷⁴ The key intermediate 8c for GABA R2/3-agonist which was used for treating anxiety, was furnished efficiently under the standard conditions (8c: 80%) (Eq 3, Table 5). Diflunisal is a non-steroidal drug with analgesic, anti-inflammatory and antipyretic properties similar to aspirin. The biaryl scaffold 8d, core of diflunisal, was efficiently prepared by using 5-bromo-2-chlorobenzonitrile and (2,4-difluorophenyl)boronic acid (8d: 87%) (Eq 4, Table 5).

The nicotinamide fungicide Boscalid which was developed by BASF, exhibit a broad spectrum of bactericidal activity and efficacy against various of fungal disease.⁷⁵⁻⁷⁷ One of the industrial production routes is a two-step process using 2-iodophenylaniline, 4-chlorophenylboronic acid and 2-chloronicotinyl chloride. However, the high cost of 2-iodophenylaniline led to this route less competitive. Through the EMM-SMC reaction, inexpensive 2-bromoaniline, instead of 2-iodophenylaniline, could work efficiently to provide the boscalid in 71% yield for two steps (Eq 5, Table 5).

To further explore the potential of this methodology, gram-scale operation was practically performed on 10 mmol for the synthesis of 1-(4'-methoxy-[1,1'-biphenyl]-4-yl)ethan-1-one 3a with a significant industrial value in 92% isolated yield (2.08 g) (Scheme1).

With regard to this solid-state EMM-SMC reaction, the ultra-low palladium loading and highly efficient transformation of this strategy cause our interest to the reaction mechanism. Generally, the classic SMC reaction catalyzed by palladium/phosphine ligand is quite sensitive to oxygen, that's why inert gas protection is necessary; however, this procedure proceeded efficiently under air conditions with only 0.05 mol% palladium loading. Notably, Hartwig et al. reported a palladium(I) dimer catalyzed SMC which is air-stable and could be finished in 15 min.⁷⁸ Recently, Schoenebeck group reported a series of work on palladium(I) dimer catalyzed cross-coupling reactions which exhibited excellent catalytic reactivity.⁷⁹⁻⁸⁵ Inspired by the pioneer work and the performance of this system, we wonder if it is possible to generate a precatalyst palladium(I) dimer *in situ* under EMM conditions. So we utilized XPS analysis to characterize the changes of valence state of palladium during the reaction (Figure 2). In the blank sample, Pd(OAc)₂ (1.0 equiv.) was mixed with DavePhos (1.5 equiv.), and the XPS analysis of Pd 3d_{5/2} shows the binding energy value of 336.93 eV, which is assigned to Pd(II) species (Figure 2a). When substrates 1a and 2a were subjected to the catalyst system for 10 min, a new curve shows that the binding energy value of Pd 3d_{5/2} shifts from 336.93 eV (Pd²⁺) to 336.06 eV which is assigned to Pd⁺ 3d_{5/2} (Figure 2b, curve in light green). Meanwhile, the binding energy value of Pd⁰ 3d_{5/2} at 335.5 eV was also detected (Figure 2b, curve in pink). After the reaction was finished, the signal of binding energy value of Pd⁰ 3d_{5/2} (335.5 eV) was enhanced obviously indicating the increasing of Pd⁰ (Figure 2c, curve in pink). These results strongly indicated Pd^{II} complex was reduced to Pd^I during the transformation, however, we could not confirm if a palladium(I) dimer was involved or not. Although we performed a series of control experiments to capture

some radical intermediates using free radical scavenger or isolate key intermediates, the highly reaction efficiency and ultra-low catalyst loading made it difficult to obtain more information, and the mechanism is still unclear.

Very recently, Galán-Mascarós⁸⁶, Kiciński⁸⁷, Chatenet/Carrey⁸⁸ and Ding⁸⁹ successively demonstrated that an external magnetic field could significantly enhance the catalytic activity of catalysts in the oxygen reduction reaction (ORR) and oxygen-evolution reactions (OER). Galán-Mascarós found a trend with a negligible effect for non-magnetic catalysts but maximum enhancement for highly magnetic ones in the magnetic nature of the catalysts. In this catalysis, the catalytic activity of possibly involved magnetic palladium(I) complex might be enhanced under the magnetic field via promoting the electron transfer. To investigate the effect of magnetic field to the SMC reaction, three control experiments were performed in toluene at different temperature without magnetic field (Table 6). Under the EMM conditions for 1 hour, 3a was isolated in 99% yield (Entry 1), however, the yields decreased sharply when the reaction were conducted in toluene. Only 27% yield of 3a was obtained with 66% 1a recovered at room temperature (Entry 2). When the reaction was heated to even 80°C, the coupling reaction could not be finished with 21% of 1a recovered (Entries 2-4). Notably, the reactions performed in toluene generated homocoupling products 3a-2 in 7%, 10%, 12% respectively. However, the homocoupling was totally suppressed under the EMM conditions. All of these results indicated that the EMM conditions could enhance the catalytic activity significantly.

Table 6. The Comparison of EMM with Solvent-based Reaction.

Entry	Solvent	T/	3a%	3a-2%	Recover of 1a%
1	-	-(EMM)	99	-	-
2	Toluene	rt	27	7	66
3	Toluene	55	46	10	49
4	Toluene	80	75	12	21

^aIsolated yield. ^bConditions A: 1-8(1.0 mmol), 2-8(1.2 mmol), Pd(dppf)Cl₂ (0.0005 mmol), DavePhos (0.00075 mmol), KF (3.0 mmol), in a flat bottom flask (10 mL) with ferromagnetic rods (5 g), EMM, 50 Hz, 3 h.

In summary, we have developed the first EMM promoted solid-state SMC reaction using a catalytic system consisting of Pd(dppf)Cl₂/DavePhos. While few previous ball-milling palladium-catalyzed solid-state coupling reactions have been reported, the substrate scope limitation, low conversion rates, using of

molecular dispersants and high palladium loading significantly limit their application. Under this EMM system, the solid-state SMC could be successfully achieved using ultra-low catalyst loading (0.05 mol%) without any molecular dispersants. This strategy shows broad substrate scope, good functional groups tolerance and efficient gram-scale synthesis. Furthermore, its utility was exemplified in the modification of photoluminescence molecules, cross-coupling of slightly soluble compound and synthesis of several important bioactive molecules. Then, the XPS analyses on the oxidation state changes of palladium catalyst suggest the involvement of Pd^I intermediate which might be the active catalytic species. Compared with the EMM-SMC, solution-based conditions afforded relative lower yields within same reaction time; even so, homocoupling byproduct was also detected. Although the results indicate EMM system exhibit excellent catalytic efficiency, the effect of magnetic field is still unclear. Finally, we anticipate that this solvent-free solid-state EMM-SMC could be developed into industrially attractive and environmentally friendly routes, and the EMM system developed in this study could unlock broad areas of chemical space for solvent-free solid-state metal-catalyzed syntheses of valuable targets in various scientific fields.

Data availability

The processed experimental data generated in this study have been deposited in the figshare database at:

Declarations

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Author contributions

H.L. and Z.Z. designed the research. L. Z. and Y. D. performed the research. Q. L., D.Z. and L.C. analysed the data, and X.L. and Y.L. wrote the paper.

Competing interests

The authors declare no competing interests.

Additional information

Supporting information. The online version contains supplementary material available at:

Correspondence and requests for materials should be addressed to H. L or Z. Z.

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Scheme

Scheme 1 is provided in the Supplementary Files section.

Figures

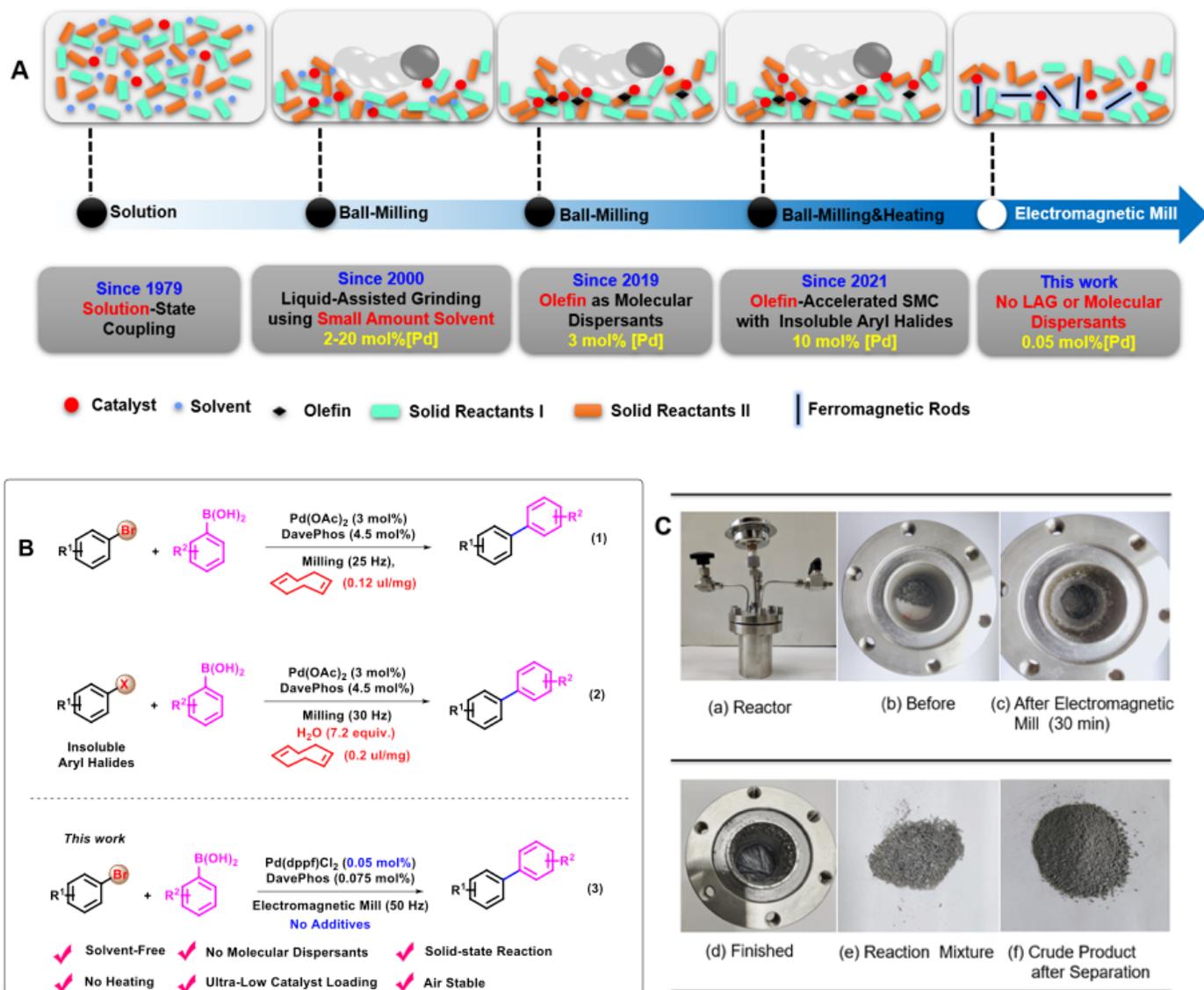


Figure 1

Suzuki–Miyaura Cross-Coupling of Solid-state Reactants using Mechanochemistry. (A) Chronology of Suzuki–Miyaura Cross-Coupling for Solid-state Reactants. (B) Recent Progresses in SMC with Broadened Substrate Scope. (C) The appearance state of Electromagnetic Mill in a stain-less-steel milling jar.

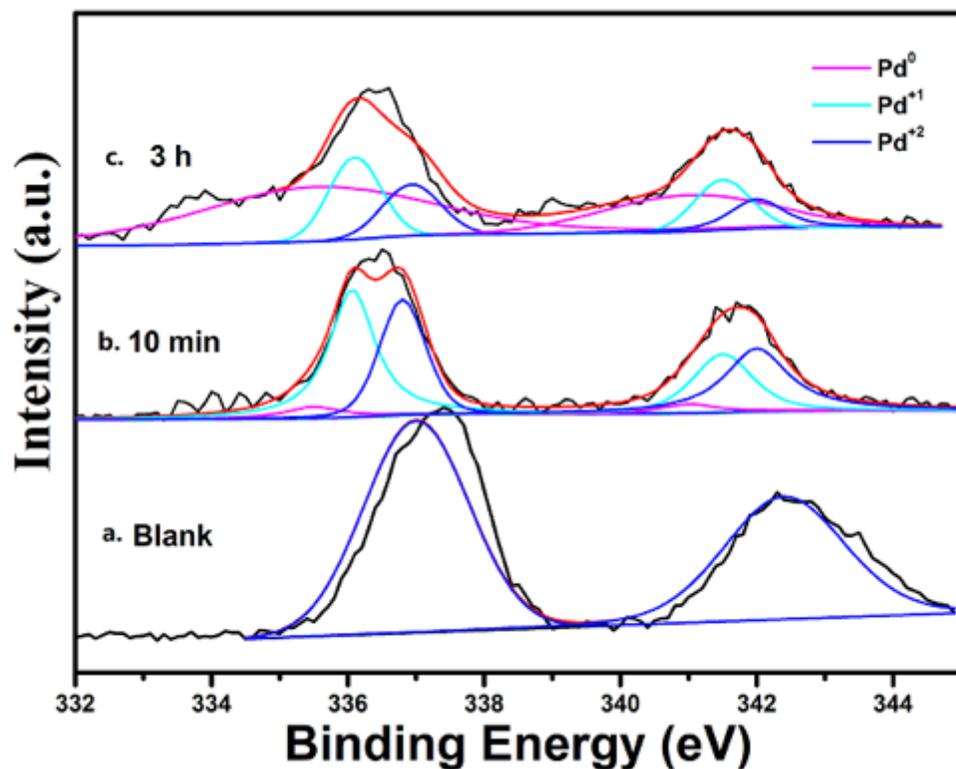


Figure 2

X-Ray Photoelectron Spectra of the Palladium Catalyst Samples. a. Blank sample: Pd(OAc)₂ mixed with DavePhos; b. Pd(OAc)₂(7 mol%)/DavePhos(10 mol%) reacted with 1a(1.0 mmol) and 2a(1.2 mmol) for 10 min; c. Pd(OAc)₂(7 mol%)/DavePhos(10 mol%) re-acted with 1a(1.0 mmol) and 2a(1.2 mmol) for 3 h.

Supplementary Files

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