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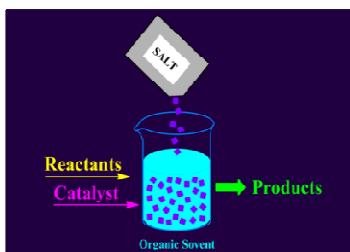
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Acceleration of Suzuki coupling reaction by abundant and non-toxic salt particles

Binbin Zhang, Jinliang Song, Huizhen Liu, Jinghua Shi, Jun Ma, Honglei Fan, Weitao Wang, Peng Zhang and Buxing Han*

Simple salt particles and Pd catalyst in organic solvents have excellent synergistic effect for promoting Suzuki coupling reactions.



Cite this: DOI: 10.1039/c0xx00000x

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ARTICLE TYPE

Acceleration of Suzuki coupling reaction by abundant and non-toxic salt particles

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

Enhancement of reaction efficiency using non-toxic, abundant, and cheap additives is an interesting topic in green chemistry. In this work, we conducted the first work to study the effect of salt particles on organic reactions in different solvents, in which the salts are not soluble, and it was discovered that NaCl, KCl, Na₂SO₄ and K₂SO₄ particles could accelerate Suzuki coupling reactions catalyzed by Pd nanocatalysts considerably. X-ray photoelectron spectroscopy (XPS) and Fourier transform infrared spectroscopy (FT-IR) studies indicated that there exist strong interactions between the salts and the catalyst (Pd) and between the salts and the reactants, which are important reasons for the synergistic effect of the catalyst and the salts. Application of salt particles suspended in organic reaction systems may become a useful strategy to develop new and green reaction routes.

1. Introduction

Many simple inorganic salts, such as sodium chloride, sodium sulfate, potassium chloride, potassium sulfate are cheap, abundant, non-toxic and chemically inert to organic reactions. The salts are widely used in different fields. As additives, salts dissolved in solutions can accelerate some organic reactions.¹⁻⁷ For example, Diels–Alder cycloadditions in lithium perchlorate–diethyl ether were accelerated significantly when compared with the salt-free organic solvent-based reactions.⁸ Alkali and alkaline earth metal salts dissolved in methanol and acetonitrile had notable effect on the rates of the α -tocopherol regeneration reaction of ubiquinol-10.⁹ The Baylis–Hillman reaction was shown to be accelerated in salt solutions of water and the “water-like” structured solvents, such as formamide and N-methylformamide.¹⁰ Salts in solution were found to have considerable impact on endo/exo ratios of Diels–Alder reaction products in both aqueous and nonaqueous salt solutions.¹¹⁻¹³ Dissolved salts were also reported to influence monomolecular heterolysis reactions,¹⁴ nucleophilic substitution reactions,^{15, 16} proton-transfer reactions in the 3,5-dinitrohydroxybenzoic acid/ammonia system,¹⁷ Wittig reaction on water,¹⁸ solvolysis reaction,¹⁹ the reaction of Glc with amino acids and peptides,²⁰ etc. Generally, the effect of salt in solution on organic reactions are attributed to the influence of ions on hydrophobic packing, solvent pressure, hydrogen bonding, hydrophobic hydration, and salting-out and salting-in effects, etc.^{3, 11, 21} Recently, NaCl aqueous solution are reported to improve depolymerization of cellulose catalyzed by organic acid because the salt in the solution enhances the disruption of the hydrogen-bond matrix among cellulose fibers.²²

It is well accepted that in a salt solution each anion or cation is surrounded by a number of solvent molecules to form solvent shell, while inorganic salt particles belong to typical ionic crystals. In the ionic crystals, as surface ions do not have its outer layer of ions, the crystal surface is partially charged,^{23, 24} as shown schematically by Figure S1 in Supplementary Information. The partially charged ions or dipoles may affect some organic reactions significantly. But the effect of solid salt particles on organic reactions should be different from that in salt solutions. To date, study of the effect of inorganic salts on organic reactions is limited to their solutions. Whether the salt particles in organic solvents affect organic reactions is unknown.

In this work, we studied the effect of suspended salt particles in organic solvents on organic reactions for the first time. It was found that NaCl, KCl, Na₂SO₄ and K₂SO₄ particles could considerably accelerate Suzuki coupling reaction catalyzed by Pd nanoparticles, which is a very powerful route for the formation of C-C bond.²⁵⁻²⁷ Further study indicated that the partially charged salt surface interacts strongly with the catalyst and the reactants, which are the important reasons for the synergistic effect of the catalyst and the salts.

Experimental

Materials: Bromobenzene, phenylboronic acid, 4-bromonitrobenzene, 4-bromotoluene, di-n-butyl ether, potassium hydroxide were all analytical grade and were purchased from Alfa Aesar China Co., Ltd. Sodium chloride, sodium sulfate, potassium chloride, potassium sulfate, benzene, and toluene were analytical grade and were provided by Beijing Chemical Reagent Company. The catalyst Pd/C was purchased from Baoji Rock Pharmachem Co., Ltd., China (5 wt% Pd, Product No. D5L3),

which had a BET surface area of $1202 \text{ m}^2 \cdot \text{g}^{-1}$ and a pore volume of $0.82 \text{ cm}^3 \cdot \text{g}^{-1}$, and the detailed characterization of the catalyst was provided previously.²⁸ For all the salts, the particles between 40 and 50 meshes were used in the reactions.

Suzuki coupling reactions: As an example, Suzuki coupling reaction of bromobenzene and phenylboronic acid is described because other reactions were similar. In a typical experiment, bromobenzene (2 mmol), phenylboronic acid (2.5 mmol), KOH (8 mmol), Pd/C (0.7 mol % relative to bromobenzene), inorganic salt, and solvent (6 mL) were charged into a flask of 50 mL equipped with a magnetic stirrer and a reflux condenser. The reaction mixture was stirred at 100°C for 1 h. After the reaction, the reaction mixture was cooled to room temperature. Then inorganic salt and the catalyst were removed by centrifugation. The quantitative analysis of the reaction mixture was conducted using a gas chromatography (GC, Agilent 6820) equipped with a flame ionization detector (FID) and a PEG-20M capillary column (0.25 mm in diameter, 30 m in length) using benzene as the internal standard. Identification of the products and reactant was done using GC-MS (SHIMADZU-QP2010) as well as by comparing the retention times of the standards in GC traces

X-ray photoelectron spectroscopy (XPS): To prepare the Pd/KCl sample, PdCl_2 (0.2 g) and NaCl (4 g) were mixed and grinded. The mixed powder was then calcined at 800°C in a quartz tube under Argon protection. The prepared PdCl_2/KCl solid was then grinded to power, followed by reduction in the flow of hydrogen at 150°C . To prepare the corresponding Pd particle, the Pd/KCl was washed to remove KCl. The X-ray photoelectron spectroscopy data were obtained with a Thermo ESCALAB250 Xi electron spectrometer from VG Scientific using 300W $\text{AlK}\alpha$ radiation. The base pressure was about 1.68×10^{-9} mbar. The binding energies were referenced to the C1s line at 284.8 eV from adventitious carbon.

FT-IR study of reactant/salt interaction: 1 μL of bromobenzene was dropped on a sodium chloride plate of 13 mm in diameter and 0.5 mm in thickness, which was prepared at 10 MPa. The FT-IR spectrum of the as prepared sample was recorded on a BRUKER TENSOR27 instrument with the sodium chloride plate as background.

2. Results and Discussion

We carried out the Suzuki coupling reaction of bromobenzene and phenylboronic acid (Scheme 1) in toluene with and without NaCl, KCl, Na_2SO_4 and K_2SO_4 particles. The characterization of the commercial Pd/C catalyst used was provided in detail in our previous paper.²⁸ Toluene was used as the solvent in order to avoid dissolution of the salts, and the results are shown in Figure 1. No by-product was detected in the reaction. For all the salts, the yield of the product increased steadily with the amounts of the salts, and their effects follow the order of $\text{Na}_2\text{SO}_4 > \text{KCl} > \text{NaCl} \approx \text{K}_2\text{SO}_4$. Our experiments showed that without the catalyst (Pd/C), the inorganic salts themselves could not catalyze the reaction, indicating the synergistic effect of the catalyst and the salts.

Scheme 1. Suzuki coupling reaction of bromobenzene and phenylboronic acid.

We studied the effect of the salts on Suzuki coupling reaction in di-n-butyl ether, and the reactions of other substrates in toluene, and the results are presented in Table 1. To show the effect of the salts clearly, the experiments were conducted in a shorter time with low conversion. The data in the table illustrates that the salt particles could also accelerate the reactions of the substrates considerably in different solvents although the extents of the effect in different solvents are different.

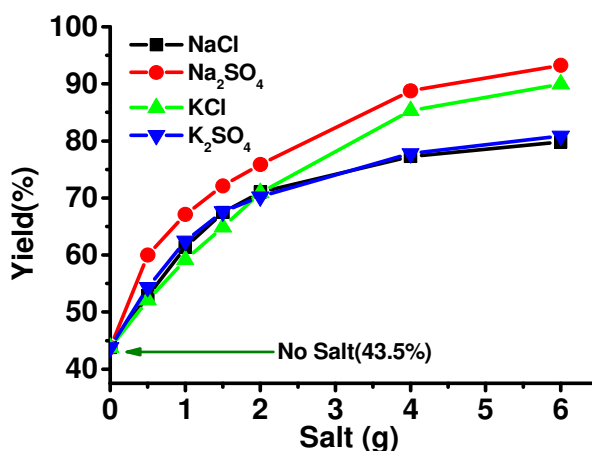


Figure 1. Effect of salts on Suzuki coupling reaction of bromobenzene and phenylboronic acid. Reaction conditions: 2.0 mmol bromobenzene, 2.5 mmol phenylboronic acid, 6 mL solvent, 8.0 mmol KOH, Pd/C (5 wt%, 0.7 mol% Pd relative to bromobenzene), 100°C , 1 h. Yields were determined by GC analysis with benzene as an internal standard.

Table 1. Acceleration of Suzuki coupling reaction by inorganic salts^a

| Entry | Substrate | Solvent | Salt/g | Yield ^b /% |
|-------|---------------------|------------------|----------------------------|-----------------------|
| 1 | Bromobenzene | Di-n-butyl ether | 0 | 10.9 |
| 2 | Bromobenzene | Di-n-butyl ether | $\text{Na}_2\text{SO}_4/6$ | 21.7 |
| 3 | Bromobenzene | Di-n-butyl ether | NaCl/6 | 24.7 |
| 4 | Bromobenzene | Di-n-butyl ether | KCl/6 | 14.8 |
| 5 | Bromobenzene | Di-n-butyl ether | $\text{K}_2\text{SO}_4/6$ | 21.4 |
| 6 | 4-Bromonitrobenzene | Toluene | 0 | 78.4 |
| 7 | 4-Bromonitrobenzene | Toluene | NaCl/6 | 99.1 |
| 8 | 4-Bromotoluene | Toluene | 0 | 31.6 |
| 9 | 4-Bromotoluene | Toluene | NaCl/6 | 58.6 |

^a Reaction conditions: 2.0 mmol halobenzene, 2.5 mmol phenylboronic acid, 6 mL solvent, 8.0 mmol KOH, Pd/C (5 wt%, 0.7 mol% Pd relative to halobenzene), 100

^aC, 1 h. ^b Yields were determined by GC analysis with benzene as an internal standard.

The reaction mechanism of Suzuki coupling reaction has been studied extensively, which can be expressed by Figure 2.^{25, 26} Suzuki reaction consists mainly of three steps, which are oxidative addition, transmetalation and reductive elimination. Generally, the oxidative addition step is believed to be the rate-determining step.^{25, 29} For Pd-catalyzed Suzuki reaction, many ligands containing phosphorus and nitrogen atoms have been used to increase the electron density of Pd, which can accelerate the oxidative addition step, and improves the reaction rate.³⁰⁻³² In order to study the reasons for the salts to enhance the reactions, we investigated the interactions of the species in the reaction system, which are discussed in the following.

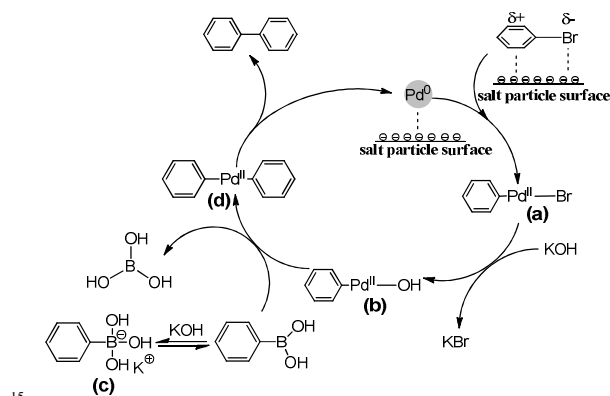


Figure 2. Suzuki coupling reaction of bromobenzene and phenylboronic acid.

We investigated the interaction between the catalyst Pd and the salts using XPS method. The XPS spectra (Figure 3) showed that Pd 3d 5/2 peaks of the Pd/KCl, and corresponding Pd particle were 335.18 eV and 335.72 eV, respectively. This indicates that the salt particles could reduce binding energy of Pd through electron-donating effect of the negative charges at the salt surface. In the reaction, the anions at the surface of the solid salt particles acted as electron donors for Pd, which increased the electron density of Pd. This effect could promote the oxidative step to form intermediate Ph-Pd^{II}-Br (a) (Figure 2). Therefore, the reaction is accelerated because this is the rate determining step. In other words, the electron-donation effect could enhance the activity of the catalyst through increasing electron density of Pd.

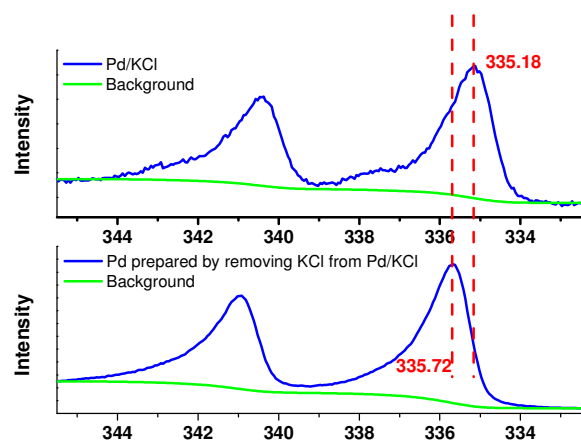


Figure 3. The Pd 3d 5/2 peaks in XPS spectra of the Pd/KCl (Pd: KCl mass ratio=1:33) and the corresponding Pd prepared by removing KCl from Pd/KCl.

We also studied the interaction between bromobenzene and the salts using FT-IR methods. Figure 4 shows the FT-IR spectra of the bromobenzene with and without NaCl. The typical unsaturated C-H stretching vibration bands are in the range of 3000-3100 cm⁻¹.³⁵ However, the bands shifted to the range of 2850-3000 cm⁻¹ after adsorbed on NaCl surface, indicating considerable interaction between bromobenzene and the salt. This may result from the electron-donating effect of the partial negative charges on the salt surface to the bromobenzene molecules adsorbed (Figure 2).

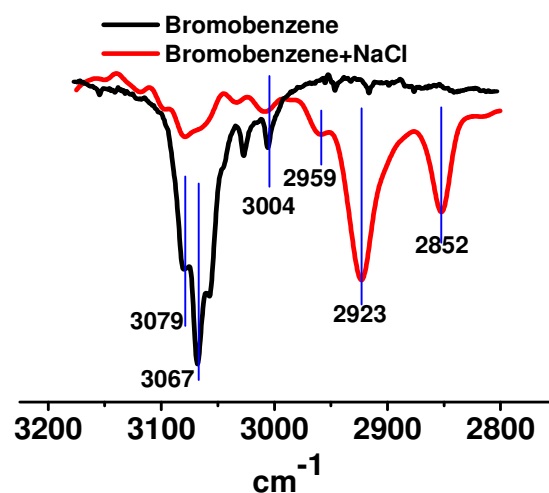


Figure 4. FT-IR spectra of the neat and adsorbed bromobenzene. The spectrum of the neat bromobenzene was measured with liquid bromobenzene in a ZnS cuvette; The spectrum of the adsorbed bromobenzene was measured with a very small amount of bromobenzene adsorbed in a pellet of NaCl, and the background was measured with the same empty pellet of NaCl.

Conclusions

In summary, the NaCl, KCl, Na₂SO₄ and K₂SO₄ particles and Pd catalyst in organic solvents have excellent synergistic effect for promoting Suzuki coupling reactions. The interactions of the partially charged salt surface with the catalyst and reactants are the main reasons for the effects. This green method to enhance the reaction efficiency has potential applications. We believe that utilization of non-toxic, cheap, and abundant salt particles as additives can also be used to enhance the rate and/or selectivity of some other reactions, which provides a simple methodology to develop new and greener reaction routes.

Acknowledgement

The authors thank the National Natural Science Foundation of China (21003133, 20932002, 21173234, 21021003), and the Chinese Academy of Sciences (KJCX2.YW.H30).

Notes and references

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† Electronic Supplementary Information (ESI) available: [Structure of
5 NaCl crystal surface]. See DOI: 10.1039/b000000x/

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