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Applications of Bases in Transition Metal Catalyzed Reactions

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Abstract

Base is usually an empirical choice in transition metal catalyzed reactions. In this review, the application of bases in transition metal catalyzed reactions is described. The major aim is to show how various bases work, and from there, how we might optimize the reaction conditions by using different type of bases, according to the specific demands in transition metal catalyzed reactions.

Keywords: anion, base, basicity, cation, transition metal catalyzed reaction

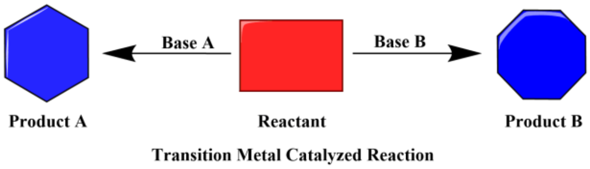
Introduction

The efficiency and yield of many transition metal catalyzed reactions are dramatically enhanced due to the addition of bases. In most work involving metal catalyzed reactions, a reaction condition screening table usually lists a number of bases and the respective yield of products. In these cases, some bases (e.g. LiO^tBu) work well to give a high yield of products while other bases (e. g. KO^tBu) afford low or even zero yield of products. Many publications show that, certain bases often works fantastic in one reaction, but makes no effect or leads to a different type of product in other reactions (Scheme 1)[1-5]. Although many studies with sporadic discussions indicate that bases play a very important role in transition metal catalytic reactions, there are few cases in literature that summarize the mechanism of bases in these kinds of reactions and answer the question as to why different bases with even similar structures lead to quite different results. As a matter of fact, based on numbers of previous work, we realized that it is very difficult to analyze and understand the influence of certain bases for a complicated reaction mixture containing several different components. The effect of bases is very complicated in many cases, which might be affected by several factors, including basicity, solubility, ionization ability, aggregation state, solvent, the size of the metal cations, Lewis acidity of the metal cations, the HSAB theory, the size of the counter anions and the coordination ability of the counter anions, etc. A base may abstract protons, neutralize acids in the reaction system, activate the catalysts and facilitate the regeneration of reactive catalytic species. The metal cation in a base may mainly influence the solubility of the base in organic solvents and the interaction with substrates or solvents. The counter anion of a base usually contribute to the coordination with a metal center and subsequently stabilize the complex. The major differences between inorganic bases and organic bases include their solubility and bulkiness. Furthermore, metal contaminants in commercial bases may also have a non-ignorable effect on the reactions, since in many cases a large excess amount of bases are added, which makes it even more difficult to eliminate their side-effect to reactions. This review is written to emphasize and summarize the mechanism of bases in transition metal catalytic organic reactions based on the limited knowledge, focusing on commonly available inorganic bases such as LiO^tBu, NaO^tBu, KO^tBu, LiOAc, NaOAc, KOAc, LiOH, NaOH, KOH, Li_2CO_3, Na_2CO_3, K_2CO_3, Cs_2CO_3, KF, CsF and organic bases such as DBU and Et_3N, etc.

Basicity, solubility and solvent

In modern chemistry, it is well known that a base contributes to the process of deprotonation and neutralization of acids during a chemical reaction.

The deprotonation ability of a base depends on its pK_a value and solubility in certain solvents.



Scheme 1

There are only a few papers reporting the solubility of different bases in various solvents (Table 1)[6]. It is also difficult to evaluate the basicity of inorganic bases in organic solvents (Figure 1)[7] due to the poor solubility of most inorganic bases in organic solvents and the aggregation between metal ions and solvent molecules, which may cause some side-effect to the basicity of bases. On the other hand, the leveling effect of organic solvents and different resolution width of various solvents make it quite complicated to study the basicity of inorganic bases in organic solvents. According to existing literature, Cs_2CO_3 has a similar basicity with DBU, while the basicity of KOH and NaO^{t}Bu are the same in organic solvents[8,9].

Table 1. Solubility of metal carbonate salts in dipolar aprotic solvents

Solvent	Li_2CO_3	Na_2CO_3	K_2CO_3	Cs_2CO_3
DMF	0.003	0.038	0.075	1.195
DMSO	0.014	0.143	0.470	3.625
DMAC	0.004	0.021	0.046	0.490
Sulfolane	0.021	0.031	0.160	3.950
NMP	0.014	0.208	0.237	7.224

Solubility in g/10 mL determined at ambient temperature by flame photometry.[6]

The solubility and basicity of bases in a reaction can result in a significant effect on results. Kobayashi et al.[10] reported the direct carboxylation of indole mediated by LiO^{t}Bu in 2012 (Scheme 2).

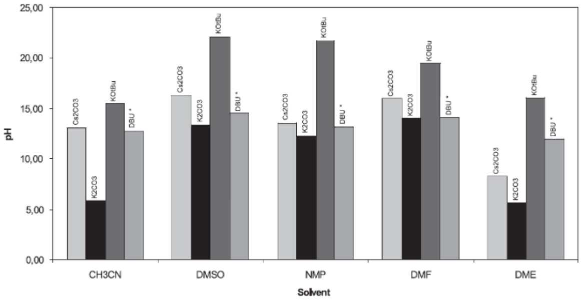
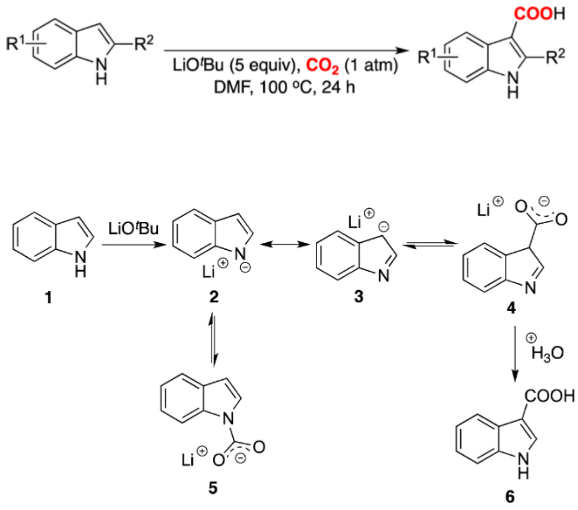


Figure 1 Basicities of cesium and potassium carbonates, potassium *tert*-butoxide and DBU in various aprotic solvents. (Reproduced from reference 7)



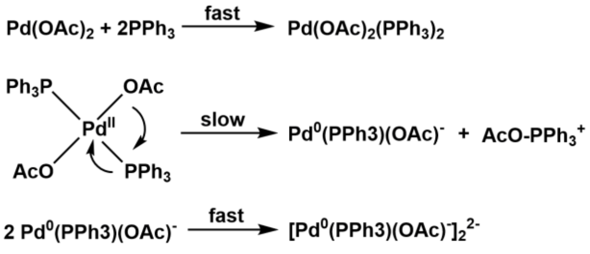
Scheme 2 (Reproduced from reference 10)

In this case different bases were chosen in the palladium catalyzed reaction system, leading to a sharp change in reaction yields. While K_2CO_3 as a weak base can only generate very little carboxyl products, Cs_2CO_3 as a strong base enhanced reaction yield dramatically. The effect of basicity also reflects on the *tert*-butyl alcohol bases, where LiO^{t}Bu with weaker basicity gave a better yield compared to stronger bases, NaO^{t}Bu, which could not produce the desired products. Although further study indicated that the metal catalyst was not necessary to the reaction, the results still demonstrated the influence of bases on reaction yields. The author also proposed a possible mechanism for this reaction that LiO^{t}Bu reacts first with the most acidic N-H bond in compound 1 to get lithium compound 2; the resulting capture of CO_2 by compound 2 gives compound 5. At a high reaction temperature, the reversible process between compound 2, 3 and 4 leads to the generation of compound 6 despite the high nucleophilicity of the nitrogen atom. However, bases with much higher basicity will be able to yield products generated from N-1 position.

Among a number of coupling reactions, base is always an indispensable part. In most of palladium catalyzed coupling reactions, Pd(0) is the active catalyst coming from Pd(II). Pd(II) can convert into Pd(0) with addition of a base. Although the mechanism of this process is still unclear, there are already some studies on the generation.

In the case of the Heck reaction, a base is usually needed to facilitate the conversion from Pd(II) to active Pd(0) species when $Pd(OAc)_2$ is used as a catalyst with triphenyl phosphine as a ligand (Scheme 3)[11-13]. Comparing to Pd(II), Pd(0) acts as a "naked" palladium species with a higher reactivity. Bases can neutralize protons generated during the conversion from Pd(II) to Pd(0) and accelerate the reaction.

Moreover, bases can also neutralize acids that result from reductive elimination, thereby speeding up the reactions and facilitate the regeneration of active catalytic species[14].

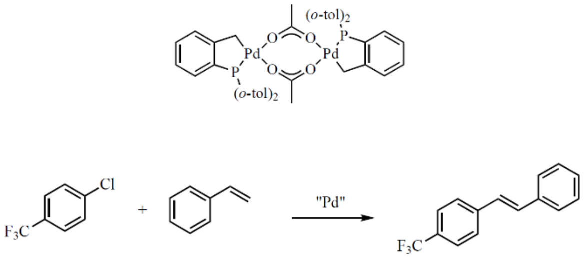


Scheme 3 (Reproduced from reference 12)

Anions

The anion in an inorganic base is usually able to act as a ligand, bonding with catalytic metal cations by filling up unoccupied coordination sites of the metal center, which will affect the regeneration of the catalyst in many organic reactions. In this way, the strength of interaction and coordination rate between metal center and anionic ligand play an important role in the reaction processes, thus reaction yield and rate usually depend on the choice of bases.

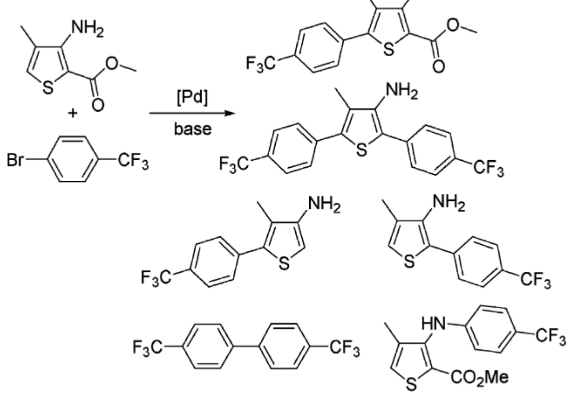
In 2001, Beller et al.[15] studied the effect of ions on the reaction shown in Scheme 4. They did a series of experiments by adding different cations and anions into the reaction to observe their effect on the reaction. The results indicated that in this particular reaction, keeping the concentration level of basic anions low could help the reaction occur more smoothly. While different anions show large differences between the results of the reaction, cations had nothing to do with the reaction aside from the solubility of the bases.



Scheme 4 (Reproduced from reference 15)

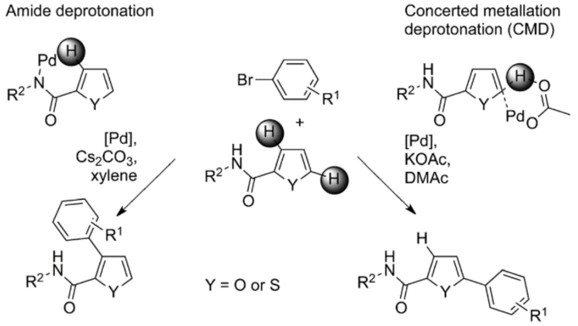
Different basic anions will not only influence the yield but also the selectivity of the reactions. Doucet et al. reported that different products were obtained by adding various bases into the same reactions (Scheme 5)[16,17].

In this reaction, Cs_2CO_3 can facilitate the generation of either products while other metal carbonates and acetates can only cause the 5-position coupling reaction to occur. The similar result was also observed by Muzart[18], but unfortunately no detailed explanation was provided.



Scheme 5 (Reproduced from reference 16)

In another study, Doucet et al. showed different results by using carbonates and acetates with the same substrates (Scheme 6)[19,20].

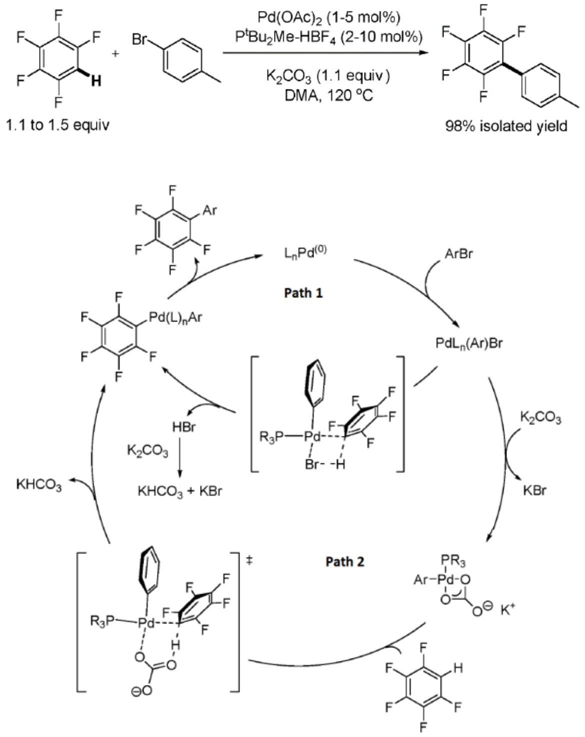


Scheme 6 (Reproduced from reference 20)

In this case the anion of a base can act as a ligand, coordinating to the metal center in a catalyst to direct the reaction. For instance, the activation reaction of C-H bond with carbonates is considered to go through a base-assisted metallation / deprotonation process. The effect of basic carbonates and acetates to the reactions in Scheme 5 could be explained by the concerted metalation / deprotonation (CMD) mechanism proposed by Fagnou et al.[21]. The base coordinates with Pd and deprotonates the substrate to activate the C-H bond. The coordination between the base and the metal center is crucial during this process. Aside from the experimental results, many computational results also demonstrate that carbonates and acetates are the most efficient bases in the activation of C-H bond. The type of reaction system determines the efficiency of a base. For example, in the reaction system shown in Scheme 6, both bases can coordinate with metal center, but the mechanisms follow a different path. The reaction results are also specifically related to the basicity of the system where the pH value has a significant impression on the regioselectivity in many cyclometallation reactions.

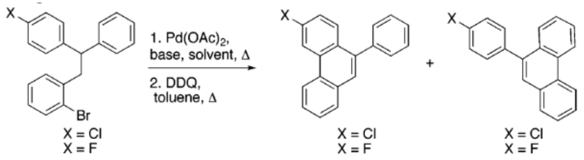
Shaw et al. found that the cyclometallation reactions of Ir[22], Pt[23] and Pd[24] complex can be accelerated by the addition of sodium acetate into the system in the early 70's. Based on this observation, in 1979, Sokolov et al.[25] reported an example of amine-directed activation of C-H bond catalyzed by chiral amino acids which ended up providing good yields and *ee* values of chiral products. They came up with a hypothesis that the most important metallation process of C-H bond underwent base-assisted intramolecular-cooperated metallation / deprotonation mechanism with a transition state.

Similar processes were observed in transition metal catalyzed reactions. Fagnou et al.[21] proposed a CMD mechanism for the reaction in Scheme 7. Under a basic condition, there are several possible pathways for the next step of oxidative addition intermediates, such as Path 1 and Path 2, which are two mechanisms of reactions between oxidative addition products and bases (Br$^-$ and CO_3^{2-}). This mechanism was first proposed by Echavarren and Maseras et al. in an intramolecular arylation reaction[26]. The only difference between them is the divergence of active catalytic species and bases for proton abstraction. In Path 1, the active species is (PR_3)ArPd-Br complex and Br abstracts a proton as a ligand. In Path 2, the Br$^-$ on Pd is replaced by HCO_3^- anion while the active species is (PR_3)ArPd-HCO_3. According to the computation result, the proton-abstraction of HCO_3^- in Path 2 has the lowest reaction energy barrier, which is also consistent with experimental data. Meanwhile, Fagnou et al. pointed out that both the basicity of bases and the ionic concentration in the reaction system have a significant influence on the reaction[27]; base assisted reactions could not take place at low ionic stength.



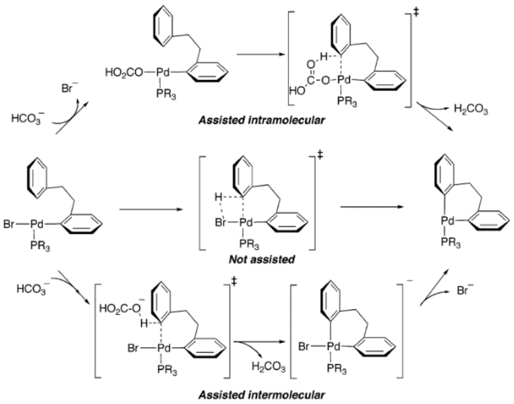
Scheme 7 (Reproduced from reference 21)

Echavarren et al.[28] also investigated the mechanism of base-assisted proton abstraction. As shown in Scheme 8, the reaction ends up with a decent yield by using K_2CO_3 as a base but gives nothing by using an organic base, such as DBU or triethylamine (TEA). The regioselectivity of this reaction depends heavily on the bases. For example, debromination product is expected as the only product when using a strong base (e. g. KO^{t}Bu). The reaction yield can be further increased by adding pivalic acid (PivOH) into the reaction system.



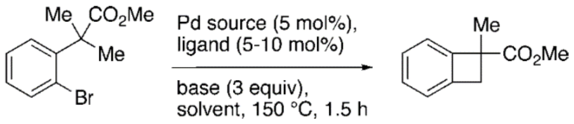
Scheme 8 (Reproduced from reference 28)

The author proposed three possible pathways for this reaction as shown in Scheme 9. From the oxidative addition intermediate, a proton can transfer onto Br (Non-base-assisted mechanism) or onto the base (Base-assisted mechanism). There are two possible pathways for a base-assisted mechanism: (i) the product is generated by a concerted deprotonation process of intramolecular coordination between Pd and CO_3^{2-}; (ii) the product is obtained through proton abstraction from the phenyl ring by free CO_3^{2-} in the system. According to the computation, non-base-assisted reaction pathway has a 20 kcal / mol higher reaction energy barrier than the base-assisted pathway, indicating that this reaction may favor the base-assisted pathway[28-30].



Scheme 9 (Reproduced from reference 28)

Baudoin et al.[31] performed a similar research (Scheme 10). The authors did a computational work on a base-assisted cyclometallation reaction; Computation results showed that the base coordinating with metal center had a significant effect on the activation of C-H bond. Based on the experiment results, K_2CO_3 was the best base, followed by $KHCO_3$, while KOAc did not show any catalytic ability. Although carbonates have a better effect in many experiment results, the models of most computation studies are still bicarbonates and acetates. The author went on to calculate the reaction energy barriers for different bases. The reaction energy barrier of OAc^- for the activation of C-H bond was found to be 138 kJ / mol, while HCO^{3-} was 143.5 kJ / mol and CO_3^{2-} 187.9 kJ / mol, which is completely contrary to the experiment data. At the same time, the computation showed that the coordination between a metal and a base, instead of Br^-, was an exothermic process with a strong thermodynamic driving force. The reaction activation energy was similar by using different bases as models in computation, however, CO_3^{2-} showed a lower reaction energy barrier in experimental studies. One effect of the bases is to coordinate with the metal center and abstract a proton.



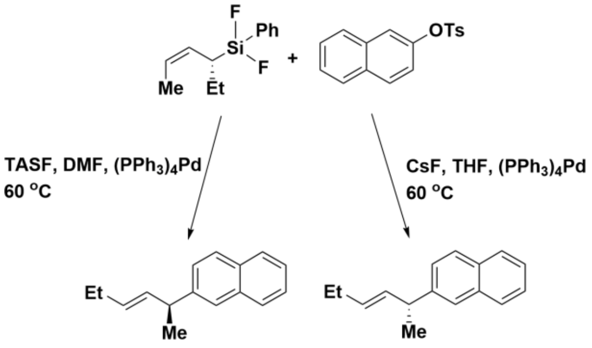
Scheme 10 (Reproduced from reference 31)

The addition of PivOH in many activation reaction of C-H bond can benefit the reaction[28,32-35], due to the insolubility of inorganic bases in organic solvents. PivOH as a soluble proton transfer reagent can transfer the proton from substrate and Pd catalyst to the bases, and gear up the reaction. Meanwhile, $PivO^-$ can also act as a ligand to coordinate with the metal center and undergo a similar reaction process as CO_3^{2-} in the activation of C-H bond.

Fluoride compounds, such as CsF and tetra-*n*-butylammonium fluoride (TBAF) are commonly used in transition metal catalyzed reactions. There are only a few solvents that can dissolve alkali fluoride compounds[36-38], but none of these solvents can be applied to all forms of fluoride compounds. Current studies about alkali fluoride compounds in transition metal catalyzed reactions mainly focus on KF and CsF. However, when KF and CsF are used in aprotic solvents, it is purposed that the reaction takes place primarily on the surface of undissolved fluoride compounds and adequately stirring is necessary to continue the reaction[38]. On the other hand, fluoride ions are able to be stabilized by the solvent molecules through hydrogen bonding in protic solvents, while the hydrogen bonding could also decrease the nucleophilicity of fluoride ions and enhance the nucleophilicity of solvents. By adding crown ether into the reaction system (such as adding 18-crown-6 where alkali fluoride compounds as bases (KF benzene or KF MeCN)[39] or nucleophilic reagents, will dramatically enhance the solubility of bases (>10x enhancement) and have a significant impact on the reaction[36].

In transition metal catalyzed reactions, fluoride compounds are usually used as bases in the coupling reactions of silicon compounds[40,41]. For instance, in the Hiyama coupling reaction, the polarization of Si-C bond is a crucial step, which needs a fluoride ion or other base to form a pentacoordinated silicious intermediate with silicon and activate the low polarized Si-R bond in organic silicon to make the consequent reaction take place. Moreover, the formation of fluoborate anion coming from fluoride ion and arylboronic acid in the Suzuki reaction can assist the reaction between borate nitermediate and Pd center. Therefore, TBAF, CsF and KF can speed up these reactions or even replace other bases used in these reactions.

Different fluoride compounds lead to various effects on the reaction due to the difference between cations, which could be used for controlling the selectivity of reactions. Hiyama et al.[41] reported that when using tris(dimethylamino) sulfonium difluorotrimethylsilicate (TASF), Pd species in the reaction will attack the double bond from the top face to form the *anti*-S$_E$ product due to the large steric hindrance of cations. However, when CsF with a smaller cation is used, the strong interaction between Pd-F-Si pushes the Pd species to approach the double bond from below to form the *syn*-S$_E$ product.

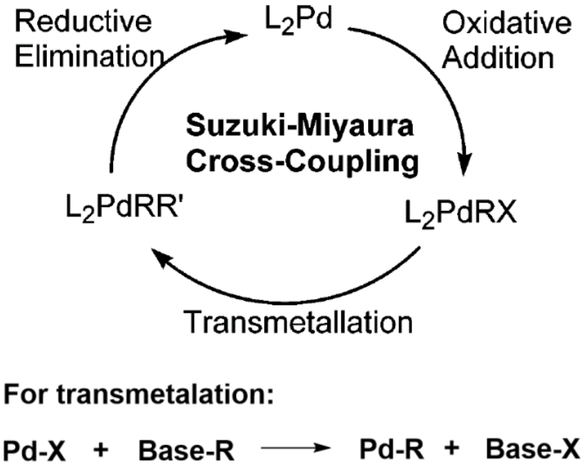


Scheme 11 (Reproduced from reference 41)

Cations

Cations also play an important role in reactions. For instance, the Suzuki reaction hardly occurs without the participation of bases. In this particular reaction, bases can help the transportation of metals (Scheme 12)[42] which not only depends on the basicit, but also has relations with the property of cations. Cations usually have various effect on the reaction, such as the size of metal cations, the HSAB theory, Lewis acidity of the metal cations, and the aggregation state in solutions. In the Suzuki coupling reaction, it is difficult to generate the ylide(Pd) intermediate if the cation is too small. Generally speaking, larger cations (e. g. Ba, Cs) can accelerate the reactions while the smaller ones have the opposite effect. The most commonly used bases in Suzuki reactions are Na_2CO_3, Cs_2CO_3, potassium acetate, potassium phosphate etc. The reactive order of alkali carbonates are as follows: Cs_2CO_3 > K_2CO_3 > Na_2CO_3 > Li_2CO_3.

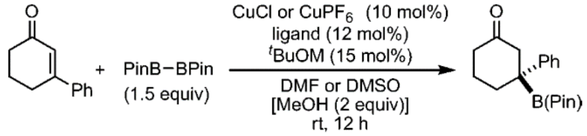
Different cations with the same anionic bases may lead to different reaction results[43,44]. Cations have an influence on the reactive intermediates; Shibasaki et al.[45] reported a reaction shown in Scheme 13 in 2009. Although LiO^{t}Bu, NaO^{t}Bu and KO^{t}Bu can accelerate this reaction, the order of yield and *ee* value was shown that LiO^{t}Bu > NaO^{t}Bu > KO^{t}Bu. The author believed that the first step of this reaction was the exchange between ^{t}BuO^{-} and the anion of Cu (I) salt to form active CuO^{t}Bu catalyst. The author speculated that cations should play a crucial role in this reaction based on the fact that the only difference between these three bases is the different cations. To prove their hypothesis, they used CuO^{t}Bu instead of LiO^{t}Bu, and foundthat the reaction could only give a 31 % yield with a 75 % *ee* value. As a control experiment, adding $LiPF_6$ into the same reaction system could end up with an 80 % yield and an 87 % *ee* value of the expected product, which indicated the importance of lithium cations in this reaction[46].



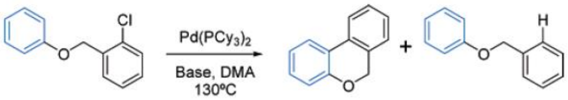
Scheme 12 (Reproduced from reference 42)

The different reaction results might be related to the various sizes of metal cations or the formation of cluster compounds between alkali metal and copper species. Meanwhile, copper salt tends to aggregate easily in strong basic environment due to the sensitivity of copper salt catalyst to the basicity of reaction system, which could slow down their reactivity, so the reaction yield and *ee* value could also be related to the basicity of bases.

Fagnou et al.[47] found that both cation and anion contributed to the yield and selectivity in the reaction shown in Scheme 14 in 2006. The reaction yield of carbonate bases are higher than the one of acetate bases, while potassium bases gave a higher reaction conversion and selectivity than sodium bases. Same anion bases with different cations showed similar selectivity in the reaction; however, organic base, e. g. triethylamine, hardly accelerated this reaction. To determine the specific role of bases in the reaction, the author compared the solubility of Na_2CO_3, K_2CO_3 and Cs_2CO_3 under the same reaction conditions. According to the results, three bases were all insoluble which indicated that the different solubility of these bases in DMA was irresponsible to the different reaction results.

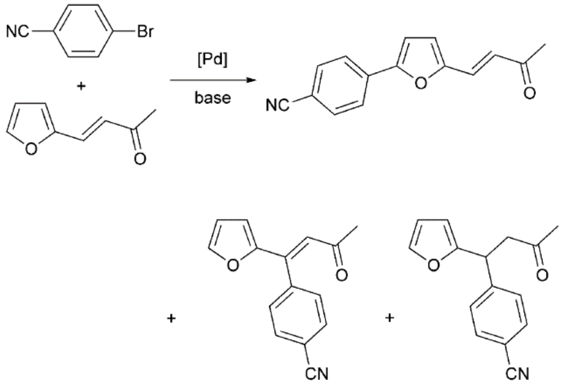


Scheme 13 (Reproduced from reference 45)



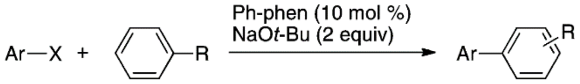
Scheme 14 (Reproduced from reference 47)

In the reaction (Scheme 15) reported by Doucet and Dixneuf et al.[48] in 2011, they discussed the influence of Na, K and Cs acetates on reaction rates (Na < K). The author thought the different yields could be explained by the CMD pathway where acetate anions in KOAc and CsOAc could approach to Pd(II) faster than the one in NaOAc and quickly generate active catalytic palladium species in the following step of hydrogen abstraction reaction. Nonetheless, this explanation was not able to answer why carbonates were not able to promote this reaction.



Scheme 15 (Reproduced from reference 48)

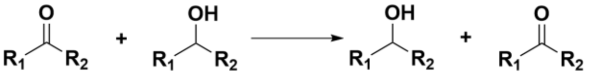
Hayashi et al.[49] studied the effect of cations in MO^tBu (M = Li, Na and K) on the reaction (Scheme 16) in 2010. In this reaction, the reaction rates enhanced as the size of ions increased by using MO^tBu (M = Li, Na and K) as a base. Compared to NaO^tBu, KO^tBu was used to give a higher reaction rate with a lower yield, which was consistent with the related single electron transfer (SET) mechanism where $^tBuO^-$ is a single electron donor, possessing higher reactivity when bonding a metal with a high electron density.



Scheme 16 (Reproduced from reference 49)

At present, there are several reports studying the effect of interaction between cations and solvent molecules or anions on reactions[50,51]. Among these studies, the interaction between cations and solvent molecules acted significant in base-promoted hydrogen abstraction reactions.

Bäckvall et al.[52] reported a reaction shown in Scheme 17 in 1991. Cyclohexanone was converted into cyclohexanol in 2-propanol in the presence of ruthenium and NaOH. According to the result, the participation of transition metal catalyst and base were indispensable in this hydrogen transfer reaction. No product was observed when only $RuCl_2(PPh_3)_3$ was added without any base at 82 °C during this reaction. Adding 2.4 mol % NaOH into the same condition could triggered this hydrogen transfer reaction from cyclohexanone to cyclohexanol with an 89% conversion (890 h^{-1} in transformation frequency) after 1 hour. It's more interesting that the transformation frequency was 1800 h^{-1} in the first 15 minutes in this reaction which was much higher than the one found in neutral conditions. The reaction can even thoroughly complete by removing acetone from reaction system.



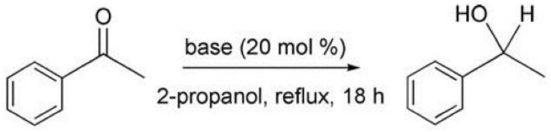
Reagents: 0.1 mol % $RuCl_2(PPh_3)_3$; 2.4 mol % NaOH

Scheme 17 (Reproduced from reference 52)

The mechanism of this ruthenium / NaOH catalyzed hydrogen transfer reaction was very similar with the one described by Cole-Hamilton et al.[53], where: (i) isopropanol anion attacked ruthenium complex first to generate an anionic active species; (ii) ruthenium-hydrogen anionic complex and acetone were obtained by elimination of β-hydrogen on alkoxy ligand; (iii) the rapid protonation of anionic species led to dihydroruthenium species, $RuH_2(PPh)_3$; (iv) cyclohexanone was reduced by dihydroruthenium species to cyclohexanol. The role of base is assisting the formation of active species $RuH_2(PPh)_3$ in this reaction.

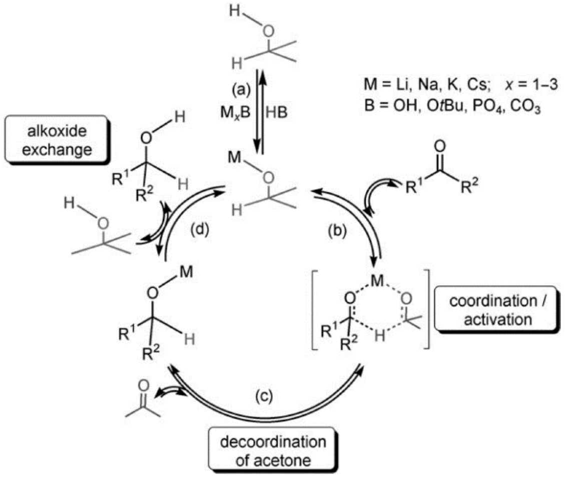
Further study of this hydrogen-transfer reactions showed that transition metal catalyst was not essential, while the hydrogen-transfer reactions could also take place in the presence of large excess amount of base[54-60]. In 2009, Varma et al.[54] found that aromatic aldehyde could be reduced in 2-propanol with KOH alone; in the same year, Ouali et al.[55] also reported that NaOH could act as an active hydrogen-transfer catalyst for some aromatic and aliphatic ketone compounds. Other bases like K_3PO_4, NaO^tBu and KO^tBu were also proved to be good candidates of hydrogen-transfer reagents for ketone compounds by many groups[56-60]. However, there are only few papers in which hydrogen-transfer reaction was promoted by catalytic amount of bases[54,55].

During the study of these reactions, Ouali et al.[55] found that different metal cations with the same anions had a positive effect on reactions (Scheme 18). Sodium bases always provide the highest yields while lithium ones only gave poor yields.



Scheme 18 (Reproduced from reference 55)

This reaction was explained by the mechanism shown in Scheme 19. At first, 2-propanol metal salt was generated through deprotonation of 2-propanol in the presence of bases (step a), which could form a six-membered ring intermediate by coordination between metal ion and oxygen atom, followed by a hydrogen-transfer to metal salt species and releasing an acetone molecule (step c). The alcohol salt then reacted with 2-propanol to obtain the expected alcohol product and regenerate 2-alcohol metal salt species (catalyst) (step d). During the first deprotonation step, no relation between the reaction and basicity of base was observed, indicating that the rate-determining step was in step b - d which could be considered as a coordination, activation and dissociation process of Lewis acid (metal ion M) and Lewis base (ketone or alcohol salt). The rate of this reaction is controlled by the strength of M-O bond[61]. In step b, harder acids tend to coordinate (Li > Na > K) while softer acids prefer to dissociation (K > Na > Li). The sodium ion shows a better balance of reactivity in these two processes, leading to the best reaction results[62,63], which demonstrating that the coordination between metal center of inorganic bases and solvent or substrate molecules has a significant effect on the reaction.



Scheme 19 (Reproduced from reference 55)

Comparison of organic and inorganic bases

The choice of bases is critical in transition metal catalyzed reactions. Organic and inorganic bases are both used widely in various reactions. However, in some reactions, the results could be quite different due to theproperties of two kinds of bases.

For example, K_2CO_3 and DBU show similar basicity but quite different reactivity in DMF. In the reaction shown in Scheme 8, Echavarren et al. [26,28] reported in 2007 that high yield of products was obtained by using K_2CO_3 as the base while the reaction did not result favorably by using DBU as base. The large steric hindrance of DBU might be the reason of unfavorable reactions.

The different solubility of organic and inorganic bases could bring in different reaction results. The actual basicity of organic and inorganic base solutions depends on their solubility in organic solvents[64,65], leading to different yields in the same reaction.

Conclusion

Bases show a number of applications and many effect factors in organic reactions. Besides basicity, solubility, ionization, effect of cation and anion as well as the difference of organic and inorganic bases, there is also experimental condition effects. The commercial available reagents usually contain tiny amount of transition metal residue. The large excess of bases used in most reactions give rise to the result that the catalytic amount of transition metals might also effect some of the reactions[55]. The tolerance of functional groups, stability of bases with other reagents and other side reactions caused by bases should also be considered for the choice of bases in addition to the intrinsic properties.

Although minimal, there is some detailed study on the roles of bases in transition metal catalyzed organic reactions at present, which mainly focuses on activation or functionalization of C-H bond and hydrogen-transfer reactions, rarely related to cations of bases, especially alkali and alkaline-earth metals. However, they usually have significant effect on reaction process due to their interactions with reaction intermediates or catalytic reactivity as a part of active species. There are many other factors of bases to effect a reaction, such as the size of metal cations, density distribution of electron cloud and interaction with the active catalyzed species. Only few papers on this field were reported due to the difficulty of trapping the intermediates during the reactions, so theoretical calculation would be an important assisted method in addition to the trapping method in the future.

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