



## Leached nickel promotes catalysis using supported Ni(II) complex precatalysts in Kumada–Corriu reactions

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### ABSTRACT

Ni(II) acetate is immobilized onto diamine ligands anchored to (i) a cross-linked poly(styrene) support and (ii) a mesoporous silica support. These anchored Ni(II) materials are successfully used to promote Kumada–Corriu reactions of 4-bromoanisole with phenylmagnesium chloride. Leaching studies utilizing filtration tests, analysis of recycle kinetics, elemental analysis, selective poisoning tests, and “three phase tests” indicate that an active catalytic species is associated with leached, soluble nickel. The cause of leaching is associated with the presence of the Grignard reagent. The use of anchored 3-iodopropyl groups for “three phase testing” of heterogeneity in Kumada–Corriu reactions is demonstrated. Polymer bound triphenyl phosphine is presented as a material for selective poisoning of soluble nickel in Kumada–Corriu reactions.

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### 1. Introduction

Metal-catalyzed carbon–carbon bond forming reactions are an indispensable tool for the synthesis of fine chemicals and pharmaceutical compounds. In 1941, Kharasch et al. reported the combined use of NiCl<sub>2</sub> and bromobenzene to promote the formation of biphenyl from phenylmagnesium bromide [1]. It was not until the early 1970s that a variety of other transition metal-catalyzed cross coupling reactions of practical use were discovered. These works set the stage for a tremendous amount of scientific investigation into metal-catalyzed cross coupling reactions. One of the first cross coupling reactions discovered during this time was the nickel catalyzed reaction of sp<sup>3</sup>-hybridized and sp<sup>2</sup>-hybridized carbons with nucleophilic Grignard reagents, almost simultaneously reported by Kumada and Corriu [2,3]. Following these original works, the literature regarding Kumada–Corriu reactions is relatively sparse as compared to the vast amount of studies regarding other C–C coupling reactions such as the Heck and Suzuki reactions. This is most likely due to the difficulty in working with Grignard reagents, which typically have stability issues and low functional group tolerances. However, the development of Kumada chemistries is of practical interest. Commercially desirable alkyl and aryl chlorides more readily undergo C–C couplings catalyzed by nickel under Kumada–Corriu conditions than under Heck and Suzuki conditions

[4]. Grignards are often used as building blocks for the formation of boronic acids, which are subsequently used in Suzuki coupling reactions. In these cases the direct use of Grignards would reduce the number of synthetic steps [5]. Kumada–Corriu reactions have found practical use in the synthesis of commercially relevant molecules, as demonstrated in a number of patents, [6] and have been used on the commercial scale to synthesize fine chemicals [7]. Of economic interest is the demonstrated ability to perform Kumada–Corriu reactions at or near room temperature, thereby reducing energy costs.

The majority of nickel catalyzed Kumada–Corriu reactions of aryl halides with Grignard reagents have been performed with homogeneous catalysts. Examples include ligandless nickel [8] and nickel complexed to phosphine ligands [2,3,9–19], bis(pyridyl)-silane ligands [20], phosphine sulfide ligands [21], N,N,O-Chelating ligands [22], allylic groups [23], carbenes [24] and imidazolium derived ligands [25,26]. Despite the high activities that can sometimes be achieved with homogeneous catalysts, the difficulties and high costs associated with recovery and reuse of homogeneous catalysts can hinder their commercial utilization. Thus, heterogeneous catalysts are often preferred in practical applications. An approach to develop such catalysts is to anchor coordination complexes to supports in the hope that they not only retain the desired catalytic properties of their homogeneous counterparts, but are also recoverable due to their attachment to an easily recovered solid.

There are a small number of studies pertaining to immobilized Ni(0) for potentially surface catalyzed Kumada–Corriu reactions. One of the first such studies was by Lipshutz et al. in which

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nickel on carbon, Ni/C, was rigorously examined for both amination and Kumada–Corriu reactions under a range of reaction conditions [27–29]. Verification of the presence of *leached*, active nickel was made by observing (i) the promotion of amination activity and the decrease in Kumada activity in the presence of PPh<sub>3</sub> immobilized on a polymer, (ii) quantification of dissolved nickel in solution by ICP–AES, (iii) effects from added homogeneous PPh<sub>3</sub>, and (iv) comparison of TONs between various metal loadings. It was also determined that leached nickel selectively partitions into the porous carbon matrix. This selective partitioning resulted in near complete recovery of metal from the recovery of the solid support material. These papers by Lipshutz et al. also stressed the danger of solely relying on ICP–AES and hot filtration experiments for determination of heterogeneous catalysis by immobilized transition metals. The topic of distinguishing homogeneous from heterogeneous catalysis will be addressed later in this work.

Styring et al. published a series of papers describing nickel anchored onto both polymer [30–32] and silica materials [33] via covalent grafting of a metal–salen coordination complex. The anchored salens were employed in Kumada–Corriu reactions to form a variety of biaryls. In one study, the elemental analyses of the post-reaction solutions showed sub-ppb levels of nickel, which was interpreted as conclusive proof for lack of nickel leaching [31]. In a later study, 1% of the nickel was found in the post-reaction solution, demonstrating that the majority of nickel could be recovered, but no claims as to the whether the reaction proceeded homogeneously or heterogeneously were made. It was noted that the catalyst could be recycled five times without significant loss in yield (no reaction kinetics were reported) [32]. Following this work, the authors immobilized a nickel–salen complex on a silica surface and used this precatalyst in a micro-flow system to catalyze the Kumada–Corriu reaction of 4-bromoanisole with phenylmagnesium bromide [33]. Again, only 1% nickel was found in post-reaction solutions, indicating that the majority of nickel could be recovered. It is our assertion that the detection of low nickel levels in post-reaction solutions does not preclude a mechanism by which metal can leach, promote catalysis, and then redeposit after completion of the reaction, as has been observed for both nickel [28,34] and palladium in other studies [35–43]. Therefore, it is unclear to what extent catalysis is happening heterogeneously or homogeneously for the nickel–salen materials, but it should be noted that these nickel–salen materials demonstrate promise as recoverable nickel sources even if they are not true catalysts for Kumada–Corriu reactions, as they can be used with low levels of nickel bleed.

This contribution describes the anchoring of Ni(acac)<sub>2</sub> onto polymer bound (1% cross-linked) ethylenediamine, *N*-(2-aminoethyl)-3-aminopropyl functionalized SBA-15 silica, and onto an 2-(4-pyridylethyl) functionalized SBA-15 silica. These materials are used as precatalysts for the Kumada reaction of 4-bromoanisole and phenylmagnesium chloride at room temperature. A series of tests are presented to demonstrate that leaching of active nickel does occur, is dependent of the presence of Grignard and does not occur to an appreciable extent in the presence of only the aryl halide. This work describes the first immobilized reagent, iodopropyl-functionalized silica, for three phase testing of anchored nickel precatalysts in Kumada–Corriu reactions.

## 2. Experimental

### 2.1. General

Reagents and solvent were purchased from commercial sources and used without further purification with the following exceptions. Dry tetrahydrofuran (THF) was passed through a packed bed

solvent system containing copper oxide and alumina columns to remove water, further dried with sodium metal under reflux, and distilled under an argon atmosphere. A commercially available 2 M solution of phenylmagnesium chloride in THF was stored in an MBraun UniLab 2000 dry box and 40 mL aliquots were transferred into a 50 mL Schlenk flask for use in experiments using standard Schlenk techniques. FT-Raman spectroscopy was performed on a Bruker FRA-106 with 1028 scans collected for each sample using a 100 kW laser source with a resolution set at 3 cm<sup>-1</sup>. GC and GC-MS analyses were performed on a Shimadzu GCMS-QP2010S with a Shimadzu SHR5 column for the flame ionization detector and a Shimadzu SHR5XLB column for the mass spectrometer detector. Simultaneous thermal analysis (Netzsch STA 409 PG Luxx) was used to determine the loadings of organically modified supports and the atomic weight percents were verified by elemental analysis (Desert Analytics, Tucson, Arizona). Large pore (105 Å) SBA-15 was synthesized according to previous reported procedures [44].

### 2.2. Organic functionalizations of SBA-15

Organic functionalizations of SBA-15 with *N*-(2-aminoethyl)-3-aminopropyltrimethoxysilane, 2-(4-pyridylethyl)triethoxysilane, and 3-iodopropyltrimethoxysilane were all performed using similar procedures.

A suspension of SBA-15 (9.0 g, 9.0 g, and 2.0 g, respectively) and dry toluene (150 mL, 150 mL, and 75 mL, respectively) was made in a 250 mL round bottom flask. To this was added the organosilane and the suspension was brought to reflux with vigorous magnetic stirring for 48 h. In the case of 2-(4-pyridylethyl)triethoxysilane 11.5 mL of doubly distilled H<sub>2</sub>O was syringed into the suspension under positive argon flow and the suspension was kept at reflux for an additional 4 h. After silane treatment the solids were filtered with copious amounts of toluene and hexanes. Soxhlet extraction of the solids was done with DCM for 3 d and the solids were dried at 75 °C to 80 °C for 16 h under high vacuum.

To cap silanol and hydroxyl groups the recovered solids from each material were each added separately to 75 mL of dry toluene to which was added 4 g of capping agent 1,1,1-3,3,3-hexamethyldisilazane, HMDS. The suspension was stirred at room temperature for 24 h and the solids were recovered by filtration and washed with toluene and hexanes. The solids were again Soxhlet extracted as described above.

STA was again performed on each material both before and after capping. Organic losses were measured between 200 °C and 800 °C.

### 2.3. Metalations of *N*-(2-aminoethyl)-3-aminopropyl functionalized SBA-15, polymer bound (1% cross-linked) ethylenediamine, and SBA-Pyridine-Ni

To 50 mL of THF was added 0.5 g of Ni(acac)<sub>2</sub>. After dissolution of the Ni(acac)<sub>2</sub>, 1.0 g of either SBA-Diamine, polymer bound (1% cross-linked) ethylenediamine, or SBA-Pyridine was added. The suspension was stirred at room temperature for 24 h, after which the solids were collected by filtration and washed with copious amounts of boiling methanol and boiling THF. The solids were then dried under high vacuum (<7 mTorr) for 16 h at 65 °C.

The colors of the final metalized materials were light blue, green, and aquamarine, respectively. Elemental analysis for the metalated SBA-Diamine showed a loading of 0.35 mmol Ni/g solids and a N:Ni ratio of 6.6 and a Ni:Si ratio of 0.03. Elemental analysis of the metalated polymer bound ethylenediamine gave a loading of 0.65 mmol Ni/g solids and a N:Ni ratio of 3.1. Elemental analysis of the metalated SBA-Pyridine gave a loading of 0.26 mmol Ni/g solids and a N:Ni ratio of 10.3 and a Si:Ni ratio of 40:1.

#### 2.4. Kumada coupling

In experiments with anchored nickel precatalysts, the precatalyst was added to a 10 mL pear shaped flask, sealed with a red rubber septum, and purged with argon for 2 min. Separately, 0.5 mmole of 4-bromoanisole and 100  $\mu$ L of diethylene glycol dibutyl ether (DGDE) were added to 4.5 mL of dry THF. This solution was syringed into the reaction flask. When homogeneous Ni(acac)<sub>2</sub> was used as the precatalyst, 0.5 mL of a 0.005 M solution of Ni(acac)<sub>2</sub> in dry THF was syringed into the flask after the reagent solution was added. The flask was partially immersed in a glass beaker with water to provide a heat sink for the exotherm from a subsequent addition of Grignard reagent and the solution was stirred for 10 min at which time a time zero sample was taken. Immediately after this, 0.5 mL of a 2 M solution of phenylmagnesium chloride in THF was injected to initiate the reaction.

#### 2.5. Reaction sampling

Samples for kinetic analysis were taken by syringing a 0.1 mL sample out of the solution. This sample was added to a solution of 1.5 mL dichloromethane (DCM) and 0.2 mL methanol. Approximately 0.2 mL of doubly distilled H<sub>2</sub>O was added and the solution was mixed by syringing in and out of a pipet a minimum of five times. The solution was allowed to separate and the DCM fraction removed via pipet, dried with MgSO<sub>4</sub>, and then passed through a cotton plugged pipet containing a small bed of celite and MgSO<sub>4</sub>. This filtered solution was then analyzed by GC. Peak identification was performed by both using standards of commercially available compounds and by using a mass spectrometer. Quantification of GC results was completed using DGDE as an internal standard.

#### 2.6. Filtration experiments

The removal of solids from reactions was performed with rigorous exclusions of water and oxygen using a swivel frit (medium frit) connected to an argon manifold on a Schlenk line. Reaction conditions for these experiments were the same as for the normal reactions with the exception that a 15 mL 3-neck flask was used as the reaction vessel and a loading of 1.0% nickel was used when the nickel-metalated, pyridine modified SBA-15 was used as the catalyst. The reaction was allowed to progress for a certain amount of time and then filtered using the swivel frit into another 3-neck flask. The filtrate was magnetically stirred and monitored for activity. Where indicated, the addition of either aryl halide or Grignard reagent was performed using a syringe.

#### 2.7. Recycle experiments

To insure enough material for elemental analysis the reaction was adjusted from that of normal runs to bring the catalyst loading to 2 mol%. SBA-Dia-Ni (100 mg) was weighed into a 50 mL round bottom flask and sealed with a red rubber septum. The flask was purged with argon. A solution of 15.6 mL of dry THF, 1.73 mmole of 4-bromoanisole, and 340  $\mu$ L of DGDE was syringed into the flask under argon flow. The suspension was allowed to stir for 10 min at which point a time zero sample was taken. A volume of 1.74 mL of a 2 M solution of phenylmagnesium chloride in THF was added to initiate the reaction. Samples were taken after 30, 120, and 240 min. After 240 min, the reaction solution was filtered and the solids were washed with methanol, diethyl ether, DCM and THF. The solids were dried at 120 °C for 2 h at ambient conditions in an oven, weighed, and then exposed to <7 mTorr vacuum for 12 h at room temperature. The mass before exposure to vacuum treatment was used as the amount of catalyst available for the next reaction and the

amount of all reagents was adjusted according to the amount of recovered catalyst. As an example, 90 mg of catalyst was recovered after the first reaction and thus 1.56 mmoles of 4-bromoanisole, 318.6 mmole of DGDE, 1.6 mL of the 2 M phenylmagnesium chloride solution, and 14 mL of dry THF, were used in the next reaction. After 2 recycles the catalyst was sent for elemental analysis.

#### 2.8. Three phase tests

Iodopropyl functionalized SBA-15, 125 mg, and the anchored catalyst were added to a 10 mL pear shaped flask, which was then purged with argon. 4-Bromoanisole, 0.2 mmole, and 100  $\mu$ L of DGDE were dissolved in ~4–5 mL THF. This solution was syringed into the flask under argon flow. When homogeneous Ni(acac)<sub>2</sub> was used as the precatalyst, 0.5 mL of a 0.005 M solution of Ni(acac)<sub>2</sub> was syringed into the flask. The final solution was allowed to stir for 10 min at which point a time zero sample was taken. A volume of 0.3 mL of a 2 M phenylmagnesium chloride solution in THF was syringed into the solution to initiate reaction. The reaction was magnetically stirred for 6 h, a sample was taken, and the solids were filtered off and washed with MeOH, diethyl ether, DCM and THF. The solids were subsequently dried at 120 °C in an oven and then analyzed by STA.

### 3. Results and discussion

#### 3.1. Synthesis of SBA-Diamine, SBA-Pyridine, and SBA-Iodine

N-(2-Aminoethyl)-3-aminopropyl functionalized SBA-15, SBA-Diamine, was synthesized by silane condensation of N-(2-aminoethyl)-3-aminopropyltrimethoxysilane onto the surface of SBA-15. The amount of tethered ligand was determined to be 1.8 mmole/g solids based on a 14.1 wt% organic loss measured by STA. The surface was capped with HMDS. FT-Raman analysis (Fig. 1) confirmed the presence of aliphatic organic groups on the surface as seen by the strong C–H stretching at 2959 cm<sup>-1</sup> and 2901 cm<sup>-1</sup> (Table 1). Unfortunately, N–H stretching bands were not observed, although this is often the case for FT-Raman spectra of tethered alkyl amines on silica surfaces. The presence of nitrogen was confirmed by elemental analysis and found to be 1.9 mmoles/g solids, which is close to the estimated 1.8 mmoles/g solids based on STA.

2-(4-Pyridylethyl)triethoxysilane was anchored onto SBA-15 (SBA-Pyridine). STA gave an estimated ligand loading of 2.8 mmole/g solids. FT-Raman spectroscopy (Fig. 1) confirmed the presence of organic species with aromatic  $\nu$ (=C–H) stretching at 3050 cm<sup>-1</sup> and aliphatic  $\nu$ (C–H) stretching is observed at 2896 cm<sup>-1</sup> (Table 1). Elemental analysis confirmed the presence of

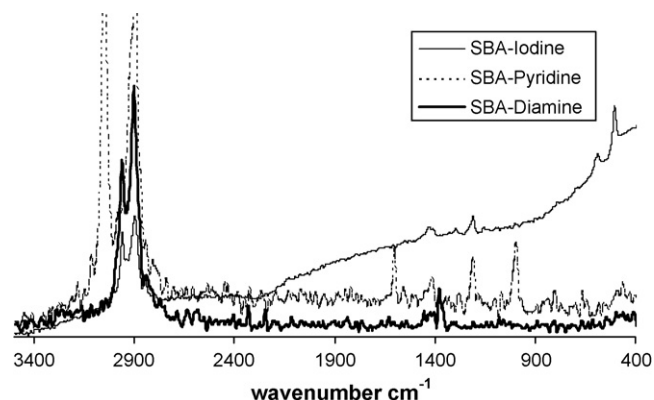


Fig. 1. FT-Raman spectra of SBA-Iodine, SBA-Pyridine, and SBA-Diamine.

**Table 1**  
FT-Raman spectroscopy peak assignments for organically modified silicas.

Material	Wavenumber (cm <sup>-1</sup> )	Assignment	Wavenumber (cm <sup>-1</sup> )	Assignment	Wavenumber (cm <sup>-1</sup> )	Assignment
SBA-Diamine	2959	$\nu(\text{C-H})$	2901	$\nu(\text{C-H})$	1376	$\delta(\text{CH}_2)$
SBA-Pyridine	3050	$\nu(=\text{C-H})$	2896	$\nu(\text{C-H})$	1601	$\nu(\text{C-C})$ aromatic
	1408	$\delta(\text{CH}_2)$	1210	$\nu(\text{C-C})$ aliphatic	992	$\nu(\text{C-C})$ aromatic
SBA-Iodine	2958	$\nu(\text{C-H})$	2890	$\nu(\text{C-H})$	1408	$\delta(\text{CH}_2)$
	1205	$\nu(\text{C-C})$ aliphatic	503	$\nu(\text{C-I})$		

nitrogen with a loading of 2.9 mmol/g solids, which is similar to the estimated loading of 2.8 mmol/g solids based on a 29.0 wt% organic loss measure by STA.

3-Iodopropyltrimethoxysilane was anchored onto SBA-15 (SBA-Iodine). The amount of tethered alkyl halide was estimated to be 1.4 mmol/g solids based on an organic loss of 27.8% measured by STA. The presence of immobilized organic and C-I bonds was confirmed by FT-Raman spectroscopy (Fig. 1). Aliphatic  $\nu(\text{C-H})$  stretching was observed at 2957 cm<sup>-1</sup> and 2893 cm<sup>-1</sup> and the peak at 503 cm<sup>-1</sup> was assigned to C-I vibrations (Table 1). The presence of iodine was also confirmed by elemental analysis, which gave loading of 1.5 mmol/g solids. This loading is consistent with the 1.4 mmol/g solids estimated by STA.

### 3.2. Synthesis of PS-Dia-Ni, SBA-Dia-Ni, and SBA-Pyr-Ni

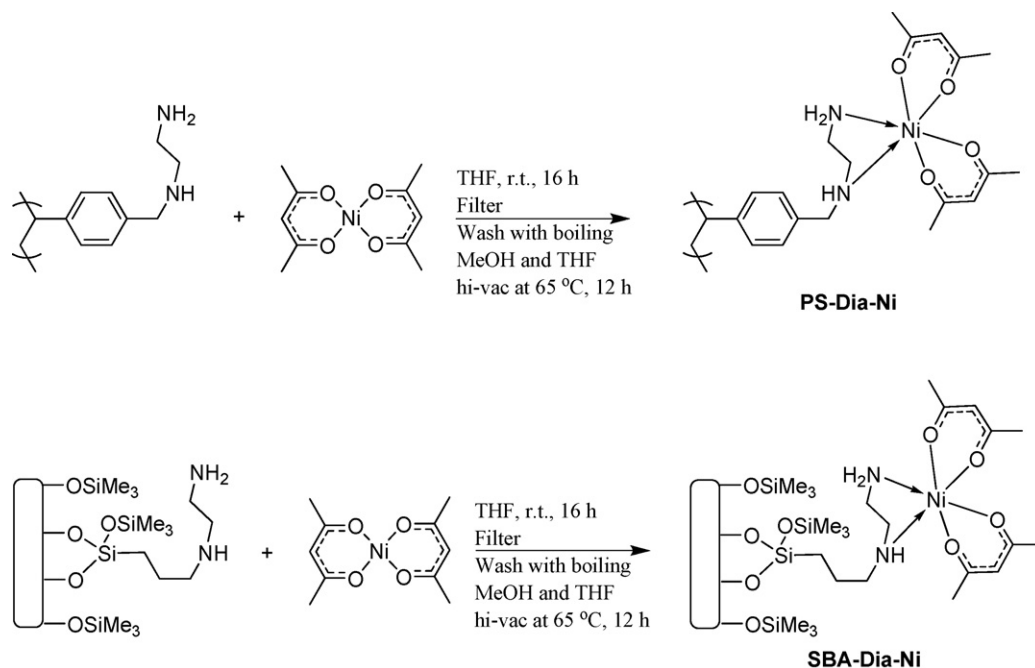
The anchoring of Ni(acac)<sub>2</sub> onto polymer-bound ethylenediamine, SBA-Diamine, and SBA-Pyridine was successfully achieved by exposing each support material to Ni(acac)<sub>2</sub>/THF solutions. Each precatalyst is respectively abbreviated PS-Dia-Ni, SBA-Dia-Ni, and SBA-Pyr-Ni. PS-Dia-Ni is green in color while both SBA-Dia-Ni and SBA-Pyr-Ni are light blue. The presence of nickel was verified for each precatalyst by elemental analysis. The homogeneous metalation of ethylenediamine with Ni(acac)<sub>2</sub> has previously been characterized by X-ray diffraction, showing an octahedral structure around the nickel atom with *cis*-arrangements of the two amine atoms and of the oxygen lone pairs of the acac ligands [45–48]. This structure is proposed, but not experimentally verified in this work, for PS-Dia-Ni and SBA-Dia-Ni (Scheme 1). Interestingly, when

homogeneous *N*-propylethylenediamine was added to a solution of THF and Ni(acac)<sub>2</sub>, the solution turned blue in color, which is consistent with the light blue color observed for SBA-Dia-Ni. The green color of the PS-Dia-Ni may be a result of either an influence of the  $\pi$ -electrons of the polymer matrix interacting with the nickel or evidence that some of the Ni(acac)<sub>2</sub> is simply entrapped in the polymer matrix, although the green color persisted after multiple washings with boiling solvents. Thus, it cannot be ruled out that some of the anchored nickel is not bound to the diamine ligand and is instead adsorbed inside the polymer matrix in PS-Dia-Ni. It is likely that Ni(II) is bound to the pyridine sites of SBA-Pyridine via the nitrogen lone pairs, but the exact pyridine-Ni(II) coordination (number of ligands per Ni) is unknown on the surface. The metalation degree suggests an excess of ligand is available.

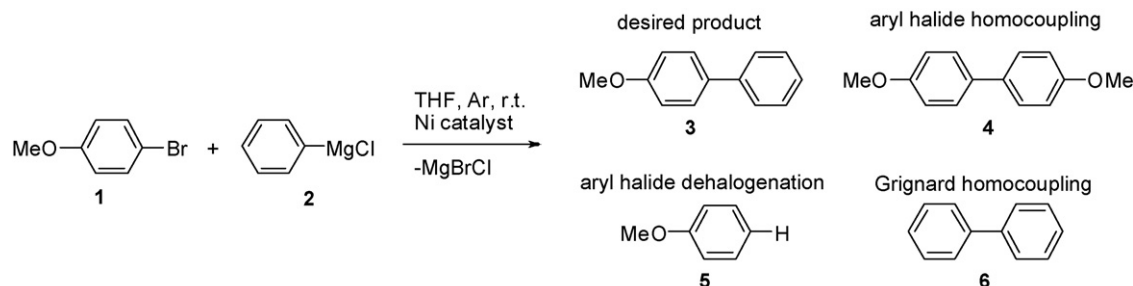
### 3.3. Activity of PS-Dia-Ni, SBA-Dia-Ni, and SBA-Pyr-Ni

The Kumada coupling of 4-bromoanisole with phenylmagnesium chloride (Scheme 2) was performed with PS-Dia-Ni, SBA-Dia-Ni, and homogeneous Ni(acac)<sub>2</sub> using a low precatalyst loading of 0.5% Ni (Fig. 2). All precatalysts allowed for good activity for the Kumada reaction with the activity increasing in order PS-Dia-Ni < SBA-Pyr-Ni, SBA-Dia-Ni < Ni(acac)<sub>2</sub>. The overall activity of each catalyst is attributed to the extent of active nickel leached into solution (*vide infra*).

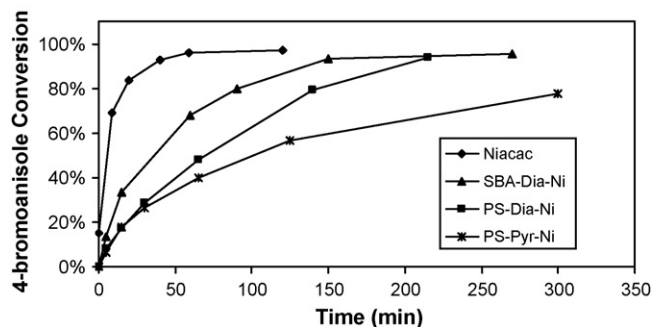
For each precatalyst studied the desired biaryl 4-methoxybiphenyl, **3**, was formed along with a significant amount of side products (Fig. 3), as was also found by previous investigators [26,28,33,49]. These side reactions include the homocoupling of



**Scheme 1.** Synthesis of anchored nickel precatalysts PS-Dia-Ni and SBA-Dia-Ni.



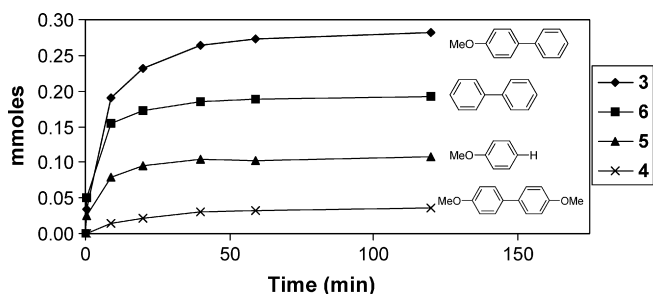
**Scheme 2.** The Kumada coupling of 4-bromoanisole (1) with phenylmagnesium chloride (2) to form desired product (3) and byproducts from aryl halide homocoupling (4), aryl halide dehalogenation (5), and Grignard homocoupling (6).



**Fig. 2.** Conversion of 4-bromoanisole using either homogeneous Ni(acac)<sub>2</sub>, SBA-Dia-Ni, SBA-Pyr-Ni or PS-Dia-Ni. Reactions were performed at room temperature under argon with 0.5 mmole of 4-bromoanisole, 1 mmole of phenylmagnesium chloride, 5 mL of THF, and 0.5% nickel catalyst.

aryl halide to form 4,4-dimethoxybiphenyl, 4, the dehalogenation of aryl halide to form anisole, 5, and the homocoupling of the Grignard reagent to form biphenyl, 6. In a control experiment without nickel present, no Kumada product, aryl–aryl homocoupling, or dehalogenation was observed to occur. However, a small amount of biphenyl, 0.02 mmole, was observed at time zero and did not increase with time. This was found to be attributable to an impurity in the fresh Grignard solution.

The increase in biphenyl, 6, with product formation, 3, was intriguing, as Grignard homocoupling was previously only thought to occur during the initial reduction of Ni(II) [34]. However, in all our experiments the biphenyl followed similar trends as shown in Fig. 3 and always ceased forming only when product formation also stopped. This observation suggests that the catalytic cycle also contributes to biphenyl formation and this has thus far not been explained in the literature. Lipshutz et al. proposed a single electron transfer, SET, to account for aryl homocoupling [29]. However, this mechanism does not explain our observation of increasing



**Fig. 3.** Comparison of the formation of product (3), biphenyl (6), and side products from dehalogenation (5) and aryl halide homocoupling (4) for homogeneous Ni(acac)<sub>2</sub> catalyzed reaction of 4-bromoanisole and phenylmagnesium chloride in Fig. 2.

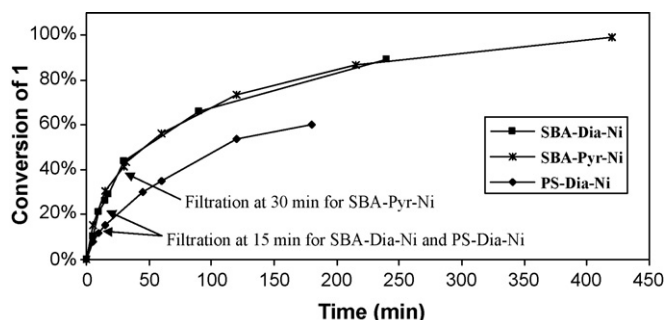
biphenyl formation with product conversion. Phan et al. have suggested that magnesium transmetalation may occur between the aryl halide and the Grignard reagent, such as between 1 and 2 [32]. In our case we see no evidence that a new aryl halide is formed, such as bromobenzene or chlorobenzene. A more fitting explanation to our data is aromatic scrambling between the nickel intermediate, Ni(II)(MeO-Ph)Br, and the starting Grignard reagent, 2. The aromatic groups may be exchanged between the Ni(II) complex resulting from oxidative addition of aryl halide and the Grignard reagent. Once the Ni(II)(Ph)X intermediate is formed it can continue in the Kumada cycle to form the Grignard homocoupled product 6. The newly formed MeOPh-Mg-X can also participate to form either desired product 3 or homocoupling product 4. Upon workup with water it can hydrolyze to form 5. A detailed analysis of the molar balances on each aryl species (Ar and Ph) in our work suggests that consideration of such scrambling may lead to mass balance closure in our system, and such a mechanism may account for the product distribution we observe [50]. Further studies would be necessary to validate or invalidate this hypothesis.

### 3.4. Filtration experiments

Having established that the anchored nickel precatalysts generate active species for the Kumada coupling of 4-bromoanisole with phenylmagnesium chloride, it is of interest to determine whether the reaction is operating heterogeneously or homogeneously. As previously mentioned, one of the most common methodologies for distinguishing heterogeneous reaction from homogeneous reaction has been the use of filtration tests<sup>1</sup> (also known as split tests) [51–53]. A very important subtlety about using this test is that only *continued activity* in the filtrate can be taken with confidence as evidence that leaching of active metal is occurring. A *lack of activity* of the filtrate in M(0) catalyzed coupling reactions cannot be taken as absolute proof that active metal did not solubilize prior to filtration, as the metal can be redeposit or deactivate during the filtration process [28,34–43,54].

Following the completions of Kumada couplings promoted by PS-Dia-Ni and SBA-Dia-Ni, the solids were filtered off via a swivel frit and fresh aryl halide and Grignard were added to the filtrate. A conversion of 74% was observed for the freshly added 4-bromoanisole, 1, in the filtrate after 100 min for PS-Dia-Ni, indicating the presence of leached active metal. A similar result was found for SBA-Dia-Ni, where 54% conversion was observed for added 1 in the filtrate after 90 min. To insure that these observations were not the result of catalyst decomposition post reaction, two tests were performed in which the solids were

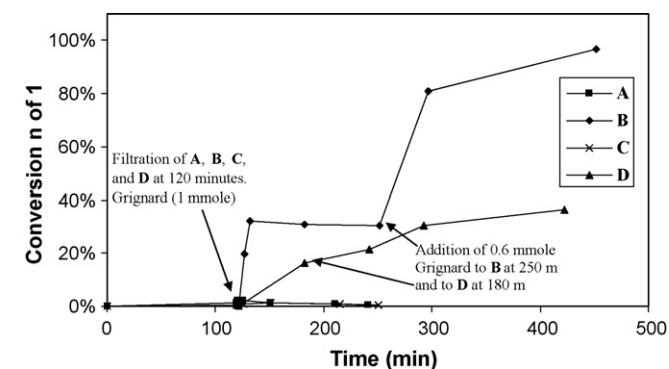
<sup>1</sup> This test is typically called a “hot” filtration test, as many catalyzed reactions are conducted above room temperature. In this study the reaction is at room temperature, which was the reaction temperature.



**Fig. 4.** Filtration tests of SBA-Dia-Ni, SBA-Pyr-Ni, and PS-Dia-Ni showing conversion of 4-bromoanisole (**1**) before and after filtration. For both reactions the catalysts were filtered off at 15 or 30 min with a swivel frit and the filtrate activity was monitored.

filtered off during the reaction cycle (Fig. 4). For both PS-Dia-Ni and SBA-Dia-Ni, the filtrates were active, although both proceeded more slowly than before filtration. A similar result was found for a reaction catalyzed by SBA-Pyr-Ni (1% nickel was used in this case) in which activity continued after filtering off the solids after 30 min (Fig. 4). The slowing of activity observed for all three filtration tests is likely a result of some Grignard deactivation, as the addition of Grignard resulted in increased activity of filtration tests (*vide infra*) in which conversion of **1** had ceased.

The cause of Ni leaching was investigated by subjecting the precatalysts SBA-Dia-Ni and SBA-Pyr-Ni to one reactant at a time. Either (i) aryl halide and THF or (ii) Grignard and THF was added to the precatalyst for two hours followed by removal of the solids under inert conditions by filtration using a swivel frit (Fig. 5). The missing reagent was then added to the solution and the conversion was monitored. In case (i) with aryl halide exposure, no activity was observed upon addition of Grignard to the filtrate, indicating that exposure to solely aryl halide is not the cause of leaching (Fig. 5A). It has been previously demonstrated for palladium catalyzed Heck reactions that Pd is leached into solution from the oxidative addition to Pd(0) when using supported Pd(0) particle precatalysts forming a soluble Pd(II) complex [55–63]. It is possible that under Kumada reaction conditions, once Ni(0) is formed, the presence of aryl halide can then oxidatively add and pull Ni(II) into solution. However, clearly aryl halide alone does not induce leaching from the supported Ni(II) complexes. In case (ii) when the



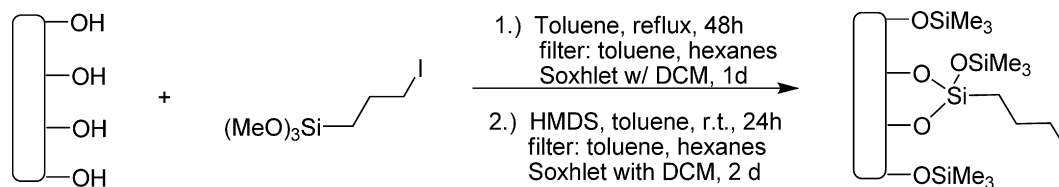
**Fig. 5.** Leaching tests of SBA-Dia-Ni with 0.5 mmole **1** at time zero (A), with filtration at 120 min followed by immediate addition of 1.0 mmole Grignard; 1.0 mmole Grignard at time zero, filtration at 120 min with addition of 0.5 mmole **1** (B); an additional 0.6 mmole of Grignard to plot B was injected at 250 min. Leaching tests of SBA-Pyr-Ni with 0.5 mmole **1** at time zero, filtration at 120 min followed by immediate addition of 1.0 mmole Grignard (C); 1.0 mmole Grignard at time zero, filtration at 120 min with addition of 0.5 mmole **1** (D); an additional 0.6 mmole Grignard was added to D at 180 min. All reactions were in THF, under argon, and at room temperature. Grignard alone is enough to induce leaching. Aryl halide alone does not.

SBA-Dia-Ni was exposed to Grignard without aryl halide, activity was observed upon addition of aryl halide to the filtrate, although it progressed at a slower rate than was observed for a normal reaction. This indicates that only the Grignard reagent is needed to leach nickel from the support. Based on the previous suggestion that a slower rate of the filtrate solution could be due to partial decomposition of the Grignard reagent during the filtration process, an additional 0.6 mmoles of Grignard was added after 250 min. After an additional 200 min (total reaction time = 450 min) the total conversion rose from 32% to 97%, indicating that some Grignard decomposition during the filtration process likely limits the conversion in the filtrate (Fig. 5B). To explore the effect of the organic modification on the leaching of nickel, SBA-Pyridine-Ni was similarly exposed to **1** without Grignard for 120 min and then filtered. Addition of Grignard reagent to the filtrate did not result in conversion of **1** (Fig. 5C). In another test, the SBA-Pyr-Ni was exposed to Grignard reagent without aryl halide for 120 min and then filtered (Fig. 5D). Addition of 4-bromoanisole to the filtrate resulted in activity (36% conversion of **1** after 420 min), confirming that Grignard exposure can generate leached, active nickel for pyridine modified silica. These results with SBA-Dia-Ni and SBA-Pyr-Ni indicate that it is likely reduction of Ni(II) to Ni(0) that promotes the leaching of nickel from the anchored nickel precatalysts. All supported precatalysts behaved similarly.

### 3.5. Three phase test

One of the more elegant methods for detection of active leached metal is the so called “three phase test”, where one of the reagents is anchored to a second solid phase (the first solid phase being the precatalyst) [55]. In this test, the only mechanism by which the anchored reagent can react (provided no significant uncatalyzed background reaction) is by leaching of the metal (or less often the substrate) from the anchored catalyst (or the anchored reagent).

As with most tests, the three phase test has some subtleties that must be taken into account before conclusions can be drawn [64]. The immobilized reagent must be sufficiently active to allow for enough observable conversion under normal reaction conditions. Therefore a control experiment in which a known, active homogeneous catalyst is added must be performed. Some amount of soluble reagent similar to (or the same as) the anchored reagent must be included to both verify that activity is possible under the three phase conditions and to mimic reaction conditions, as the presence of the soluble reagent might be required for leaching of the metal [55]. The conversion of anchored reagent is best interpreted as evidence that leaching is occurring. The absence of activity of the anchored reagent can suggest a heterogeneous pathway for the anchored catalyst only after it can be demonstrated that condition (1) above has been investigated. Even then, two further complications exist; (i) the presence of the heterogeneous catalyst can obscure the results if it serves as a deposition site once soluble reagent has been consumed, thereby scavenging active metal from solution and thus prohibiting reaction of the anchored reagent. Furthermore, (ii) the concentration of leached metal may be significantly less than what is used by a researcher in proving reactivity of the anchored reagent in condition (1), thus when the “heterogeneous” catalyst is employed, the rate of reaction of the anchored reagent is greatly reduced because the concentration of soluble metal is lower than what was used in the homogeneous activity test. These subtleties of the three phase test have previously lead to conflicting assignments of activity in Pd(0)-catalyzed Heck and Suzuki reactions using alkylthiol anchored Pd(II) precatalysts to both heterogeneous and homogeneous catalysts [56,65–67], with our accumulated data suggesting solely homogeneous catalysis [44].



Scheme 3. Synthesis of SBA-Iodine.

A three phase test for Kumada reactions has not been previously performed.<sup>2</sup> In previous works we have synthesized three phase materials for the study of palladium catalyzed Heck reactions [68,69] and other authors [70] have made similar materials bearing an aryl halide. However, the presence of carbonyl groups make these materials unsatisfactory for Kumada reactions due to propensity for nucleophilic attack of carbonyls by Grignard carbanionic alkyl groups. As such, the anchoring of a 3-iodopropyltrimethoxysilane onto a silica surface, SBA-Iodine, using traditional silane chemistry was chosen to provide a highly reactive C–I bond while avoiding functional groups that are undesirable for Grignard reagents (Scheme 3). SBA-15 was chosen as the silica material for anchoring the iodophilane as it has a large surface area for functionalization and should not interact with the supported catalyst or cause pore blocking since it is exactly the same silica material as that used for the nickel precatalysts [44].

A homogeneous control reaction of 0.5 mmole of 3-iodopropane and 1.0 mmole of phenylmagnesium chloride in the presence of 0.5% Ni(acac)<sub>2</sub> resulted in complete conversion of the iodopropane within one minute. However, only a trace amount of the Kumada product propylbenzene was observed indicating that the majority of reaction occurred through dehalogenation of the iodopropane via magnesium transfer. This is supported by the detection of a trace amount of iodobenzene and no detection of any other products (any propane resulting from formation of propylmagnesium iodide would have been lost to the gas phase during workup). The ultimate goal of the three phase test is the detection of active soluble nickel under Kumada conditions. As dehalogenation occurs concurrently with normal Kumada couplings, we suggest that the nickel catalyzed dehalogenation of anchored iodopropane can be used to detect leached, reactive nickel. Five three phase tests were performed using aryl halide, Grignard, and various catalysts. The differences in conditions/catalysts between each test included (i) no catalyst, (ii) homogeneous Ni(acac)<sub>2</sub>, (iii) SBA-Dia-Ni (0.00025 mmole Ni), (iv) PS-Dia-Ni (0.00025 mmole Ni), and (v) SBA-Dia-Ni (0.00025 mmole Ni), all without aryl halide.

After reaction the solids were recovered by filtration, rinsed with methanol, diethyl ether, THF, and DCM, and dried at 120 °C. The final dried solids were analyzed by TGA (Fig. 6) and elemental analysis. The TGA data clearly show that overall combustible mass loss due to anchored organic material is largely unaffected by the presence of either aryl halide or Grignard reagent when nickel is not present. However, in each case in which nickel is introduced, either by using homogeneous or anchored Ni(acac)<sub>2</sub>, a dramatic decrease is observed in the amount of combustible organic mass. This is consistent with the iodopropyl surface substituting an iodine atom (MW = 126.9 mg/mmmole) with either a phenyl group (C<sub>6</sub>H<sub>5</sub>, MW = 77 mg/mmmole) or a hydrogen atom. Indeed with palladium catalyzed Kumada-Corriu reactions of alkyl iodides with Grignard

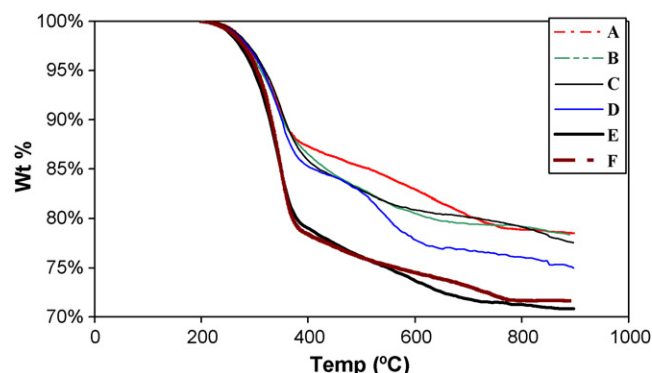


Fig. 6. TGA wt% losses (normalized to mass at 200 °C) of various used three phase materials demonstrating presence of leached nickel. In each reaction, 125 mg of the three phase material, SBA-Iodine, was exposed to (A) reaction conditions with 0.0025 mmole Ni from SBA-Dia-Ni; (B) same as (A) but without 4-bromoanisole; (C) reaction conditions with 0.0025 mmole Ni from PS-Dia-Ni; (D) reaction conditions with 0.0025 mmole Ni(acac)<sub>2</sub>; (E) reaction conditions without nickel; and (F) no reaction (unused material). Reaction conditions are 125 mg SBA-Iodine, 0.2 mmole 4-bromoanisole, 0.6 mmole Ph-Mg-Cl, and 5 mL of THF. Each reaction was stirred under an argon atmosphere for 6 h before solids were recovered. The mass of precatalyst in the solids (~5%) collected for STA analysis is inconsequential compared to the mass of SBA-Iodine and can be neglected.

reagents, the primary product was from dehalogenation and not from cross coupling [71].

Elemental analysis of the used three phase materials showed that in the control experiment without any nickel present the ratio of iodine to silicon dropped only 5% as compared to the fresh material. In the presence of nickel, the change in I:Si ratio was more substantial. When homogeneous Ni(acac)<sub>2</sub> was used, a 49% drop in the I:Si ratio was observed, and with SBA-Dia-Ni, the decrease was higher at 63%. This trend is consistent with the larger decrease observed in combustible organic mass observed in Fig. 6 between plots A and D.<sup>3</sup> Thus, SBA-Iodine can be used as a three phase material to detect the presence of leached nickel for Kumada reactions and confirms nickel leaching when used with PS-Dia-Ni and SBA-Dia-Ni.

### 3.6. Catalyst recycling

For anchored palladium precatalysts, an ability to reuse the palladium by a release and recapture strategy has been demonstrated [36–38,40–42]. In such a system the palladium atoms are leached, catalyze the reaction, redeposit back onto the surface, and are recovered by filtration of the solids. Lipshutz et al. reported that nickel on charcoal leached from the surface to catalyze Kumada couplings, but could be reused due to nickel's selective partitioning

<sup>2</sup> Lipshutz et al. report a “three phase test” in which a phosphine ligand was immobilized, which constitutes a third solid phase [35]. Calling this a three phase test is perfectly acceptable, however to avoid confusion when the term “three phase test” is used in this work, we note that we only use this term when referring to anchoring of a reagent and not a ligand.

<sup>3</sup> Despite the use of MeOH to quench and dissolve any R-Mg-X species formed on the three phase material surface, it cannot be ruled out that some potentially incombustible Mg-I species is present on the three phase materials exposed to homogeneous Ni. Thus, this test, as described in this work, is for qualitative determination of leached Ni.

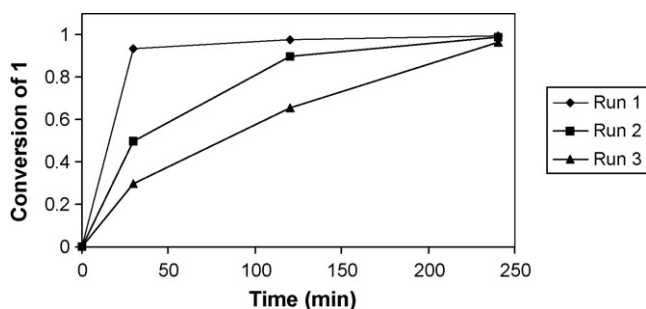


Fig. 7. Recycle experiments using SBA-Dia-Ni showing a loss in initial rates due to metal loss. Concentrations were adjusted on each run to ensure the same concentration of reagent to catalyst. Reaction is Kumada coupling of **1** with **3** with catalyst loading at 2 mol% to **1**.

inside the charcoal pores and the propensity to redeposit onto the charcoal surface [34]. To probe if such a mechanism could occur for these supported precatalysts, a series of two recycles was performed with SBA-Dia-Ni. The amount of SBA-Dia-Ni was increased from that of the normal Kumada reaction to insure enough material for elemental analysis. The first reaction was performed using 100 mg of SBA-Dia-Ni (0.035 mmole Ni), 1.74 mmole aryl halide, 1.74 mL of 2 M phenylmagnesium chloride in THF, and 15.6 mL of dry THF. It is common in catalytic coupling literature to only report the final conversion after a given period of time. However, this can result in misleading conclusions if the total reaction time is sufficiently long to hide losses in early kinetic behavior resulting from metal loss or deactivation [35,51,54]. With this in mind, data points were taken at 30 min, 120 min, and 240 min to observe changes in the kinetic profile while minimizing catalyst loss from sampling. Due to unavoidable workup losses of ~10 mg of catalyst for each recycle as determined by the mass of recovered solids, the reagent and solvent amounts were reduced by 90% and 80% respectively from the first run to insure the same ratio of reagent to nickel. After each recycle the initial rates were significantly reduced after 2 recycles (Fig. 7).<sup>4</sup> Elemental analysis after the final recycle showed a reduction of the Ni:Si from 0.03 to 0.016, which is a 47% reduction in nickel content. Thus it is possible that release and capture of the Ni is occurring, but not at a level to sustain similar kinetics for each run. Also, the large amount of nickel lost indicates that metal recovery strategies such as the use of metal scavengers would still be needed in order to purify products from nickel contamination.

### 3.7. Selective poisoning

Previously we [44,54,68,69,72] and subsequently others [56,73–76] have used selective poisons that target active, homogeneous metal to determine whether or not heterogeneous catalysis is happening concurrently with homogeneous catalysis from leached metal. In the selection of an appropriate selective poison there are a few ideally desired attributes. The selective poison should have no effect on the reagent activity or react directly with the reagents, should completely and rapidly quench soluble metal, and should have no effect on metal retained on the precatalyst surface.

<sup>4</sup> Note that if only final conversions were compared at  $t=240$  m, each run would appear to have same conversion, ca. 98%. Without evaluating the early age kinetics this might have erroneously implied retention of catalyst activity. This is a common misconception and is the greatest single flaw in the catalytic coupling literature describing supported precatalysts. Comparison of yields at long reaction times is nearly always exclusively used to assess recyclability; however, kinetic tests are the proper way to assess any catalyst.

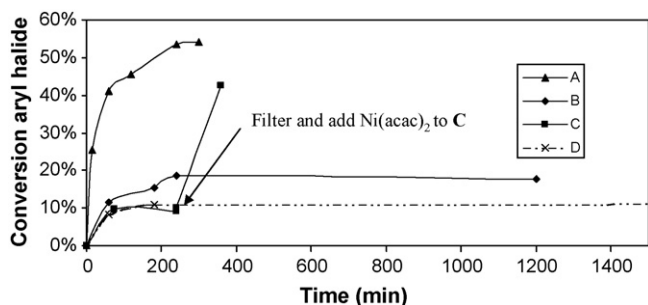
Deviations from the ideal attributes listed above can only be tolerated if the deviations are understood and do not misconstrue the interpretations of the results. The unique conditions of Kumada couplings (room temperature, use of nickel, and presence of Grignard reagents) make the development of selective poisons for such couplings an interesting challenge.

A variety of selective poisoning materials was tried for the Kumada reaction catalyzed by homogeneous Ni(acac)<sub>2</sub>. Previously we have used poly(4-vinylpyridine) to test the ability of anchored Pd precatalysts for Heck reactions [68,69,72]. When 81 mg (300 equivalents pyridine to nickel) of PVPy was added to the Kumada coupling of 4-bromonitrobenzene with phenylmagnesium chloride with 0.5% Ni(acac)<sub>2</sub> under otherwise normal conditions, the reaction reached 60% conversion of aryl halide within 30 min, but did not further react (all byproduct formation also ceased). A second reaction was run in which the amount of PVPy was increased to 200 mg. No product formation was observed. To test if the PVPy was poisoning nickel or interfering with one of the reagents, this reaction was filtered under argon and additional 0.5% of Ni(acac)<sub>2</sub> was added to the filtrate. However, no conversion was observed indicating that the PVPy was interfering with the catalysis presumably from interactions with the Grignard reagent. To test this, a third PVPy reaction was performed using 100 mg of PVPy. In this reaction total conversion after 240 min was 9% (with only small amounts of byproducts or biphenyl formed). An additional 1 mmole of Grignard was added to this reaction at 240 min and after 50 additional minutes the conversion rose to 72%. Thus, it is likely that the PVPy is predominantly interfering with the Grignard reagent and is not an adequate material for selective poisoning in this case. This suggests care must be taken in considering the use of pyridine based materials as ligands for Kumada reactions. It is reasonable to assume that when pyridine is used as a catalyst ligand, and assuming typical catalyst loadings <1%, interactions between uncoordinated pyridine sites and Grignard are not noticed or do not affect the catalysis to an appreciable extent because the ratio of pyridine sites to Grignard is small. It is postulated that only under conditions with (i) a high pyridine to Grignard molar ratio, as is the case with the PVPy poisoning test above (pyridine:Grignard ~1.0), and (ii) use of anchored pyridine that pyridine–Grignard interactions become detrimental to Grignard reactivity.

Quadrapure™ imidazol-1-yl propylaminobut-2-enoate ester (Quad IMDAZ), is an anchored imidazolium ligand on a cross-linked polymer made by Reaxa Ltd. and is reported as a good scavenger of Ni(0) and Ni(II) [77]. When 167 mg of Quad IMDAZ (100 equivalents to Ni) was added in a similar fashion as for PVPy above using Ni(acac)<sub>2</sub> as the catalyst, the conversion of aryl halide reached 75% in 240 min. Therefore, Quad IMDAZ was also rejected as a selective poison of homogeneous nickel in these Kumada reactions.

In a related experiment Lipshutz et al. noted that when polymer-bound PPh<sub>3</sub> was added to a Kumada coupling using Ni/C as the catalyst only 42% conversion of aryl halide was observed as compared to 100% without polymer-bound PPh<sub>3</sub> (PB-PPh<sub>3</sub>) [34]. This was interpreted, in combination with results from other tests, as showing that there was little or no activity from heterogeneous nickel. In contrast to the Ni/C experiments, a reverse trend was noted when NiCl<sub>2</sub> was used as the catalyst. Without PB-PPh<sub>3</sub> the reaction progressed to 60% whereas with PB-PPh<sub>3</sub> it went to 70%. No explanation for this reverse trend was given. If the PB-PPh<sub>3</sub> is truly acting as a selective poison of soluble, active Ni, then the NiCl<sub>2</sub> reaction with PB-PPh<sub>3</sub> should have been lower. Also, in the case of amination reactions, the PB-PPh<sub>3</sub> actually promoted activity, although this could be a result of the different reaction conditions employed for the amination reactions. These results raise the possibility that the PB-PPh<sub>3</sub> was interfering with the Ni/C reaction in a different way than by simply poisoning soluble Ni, such as by





**Fig. 8.** Use of PB-PPh<sub>3</sub> as a selective poison for nickel catalyzed Kumada couplings of 0.5 mmole 4-bromoanisole and 1.0 mmole phenylmagnesium chloride. Plot A is 50 mg PB-PPh<sub>3</sub> and 0.0025 mmole Ni(acac)<sub>2</sub>; plot B is 100 mg PB-PPh<sub>3</sub> and 0.0025 mmole Ni(acac)<sub>2</sub>; plot C is 100 mg PB-PPh<sub>3</sub> and 0.0025 mmole Ni(acac)<sub>2</sub> with filtration at 240 min and an additional 0.0025 mmole of Ni(acac)<sub>2</sub> added to the filtrate; and plot D is 50 mg PB-PPh<sub>3</sub> added to 0.0025 mmole of SBA-Dia-Ni.

blocking pores in the Ni/C or a potential interaction of Grignard<sup>5</sup> with polymer-bound PPh<sub>3</sub> (this latter point was not discussed in the original paper). No further experiments with PB-PPh<sub>3</sub> with Ni catalysts in Kumada reactions were conducted<sup>6</sup> and so conclusive interpretations about whether or not PB-PPh<sub>3</sub> acted as a selective poison in this previous work cannot be made using these limited data. Thus we sought to further investigate PB-PPh<sub>3</sub> as a selective poison.

Various amounts of commercially available, insoluble PB-PPh<sub>3</sub> (3.3 mmole P/g solids) were added to Kumada couplings of 4-bromoanisole and phenylmagnesium chloride catalyzed by either Ni(acac)<sub>2</sub> or SBA-Dia-Ni (Fig. 8). The addition of 50 mg of PB-PPh<sub>3</sub> to catalysis by Ni(acac)<sub>2</sub> resulted in an overall conversion of 54% after 300 min (Fig. 8A), which is a reduction from that observed with PB-PPh<sub>3</sub> (100% in 120 min, Fig. 1). Increasing the amount of PB-PPh<sub>3</sub> reduced the conversion to 19% after 240 min and stayed at this level after 1200 min of total reaction time (Fig. 8B). To test if the PB-PPh<sub>3</sub> was significantly interacting with the Grignard reagent, a second test using 100 mg of PB-PPh<sub>3</sub> was performed (Fig. 8C). After 240 min the total conversion reached 9% at which point the solids were filtered off and another dose of Ni(acac)<sub>2</sub> was added to the filtrate. A relatively rapid conversion to 43% after an additional 120 min was observed. This test indicates that the PB-PPh<sub>3</sub> does not significantly interact with the Grignard reagent compared with other potential poisons tested above and reduction of activity is more likely from interactions between the anchored phosphines and the nickel. Next, the influence of 50 mg of PB-PPh<sub>3</sub> was tested using SBA-Dia-Ni as the catalyst. After 180 min of reaction a total conversion of 11% was observed and did not increase even after a total of 2900 min (Fig. 8D). Thus, while a small amount of surface catalysis using this precatalyst cannot be ruled out, a significant fraction of catalysis is from leached metal.

It appears that the application of PB-PPh<sub>3</sub> as a solid poison of soluble metal may be used to suggest whether conversion catalyzed by leached nickel occurs. However, it did not completely cease activity in the control experiment of Ni(acac)<sub>2</sub>, and thus should be used with caution as a selective poison for nickel catalyzed Kumada reactions and further detailed work on the topic is warranted. The use of other tests for leached metal (such as filtration tests, catalyst recy-

cling, and three phase tests) is suggested to aid in the analysis of results from selective poisoning experiments using PB-PPh<sub>3</sub>.

#### 4. Conclusions

Ni(acac)<sub>2</sub> was immobilized onto (i) poly(styrene)ethylene-diamine, (ii) ethylenediamine covalently tethered to a mesoporous silica, and (iii) ethylpyridine covalently tethered to a mesoporous silica. These materials were successfully used in the catalysis of a prototypical Kumada-Corriu reaction of 4-bromoanisole with phenylmagnesium chloride. Activity from leached metal was demonstrated by both room temperature filtration tests during and after the reaction. For the first time, an anchored aryl halide (three phase test) was designed for Kumada-Corriu reactions and used to demonstrate that anchored nickel precatalysts leach active metal. It is not the presence of aryl halide that promotes leaching, but rather the presence of Grignard that pulls nickel into solution either by degradation of the ligand or reduction to Ni(0). Anchored nickel could be reused three times without significant loss in final yield, however decreases in early age activity and a 46% loss of nickel after the third run indicate that while a nickel release and capture mechanism is possible, high conversions are not sufficiently sustainable over more than three runs unless reaction times are sufficiently increased. Use of PB-PPh<sub>3</sub> as a selective poison suggests that the majority and perhaps all catalysis is associated with soluble nickel.

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<sup>5</sup> In the previous work, the phosphine to Grignard molar ratio was 0.13 and the total amount of PB-PPh<sub>3</sub> solids added was 167 mg. The amount of solvent was 1.5 mL of THF. Under these conditions it is possible that a strong phosphine-Grignard interaction was occurring.

<sup>6</sup> This is most likely due to the fact that the use of PB-PPh<sub>3</sub> was not a central point to the authors' original work as most of the PB-PPh<sub>3</sub> testing was used with amination reactions [35].

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