A polymer-supported nickel(II) catalyst for room temperature Tamao–Kumada–Corriu coupling reactions

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Dedicated to the memory of the late Alan D. Roberts

A nickel(II) co-ordination complex, covalently immobilised on a Merrifield resin, is an effective recyclable heterogeneous catalyst in a room temperature coupling reaction between a Grignard reagent and an organobromide. The immobilised catalyst does not leach metal into solution. Catalyst stability has been rationalised in terms of the combination of hard and soft donor atoms around the variable oxidation state nickel.

KEY WORDS: Kumada; catalytic cross-coupling; nickel; resin-immobilised; kinetics; catalyst recycling

1. Introduction

Metal-catalysed cross-coupling reactions have gained popularity over the past thirty years, in particular as convenient techniques for the formation of carbon–carbon bonds. The Tamao–Kumada–Corriu reaction [1] has the advantage over Suzuki [2] and Heck [3] reactions in that hybridisations of carbon other than sp^2 can be utilised in the organometallic reagent. The reaction involves the oxidative addition of an organobromide to a transition metal catalyst, which then reacts with the organometallic Grignard reagent to give the coupled product by reductive elimination. The reaction can be carried out over a wide range of temperatures from $-20\,^{\circ}C$ to refluxing solvents, however for commercial efficiency a room temperature reaction is preferable. Catalysts used in the reaction are generally based on either homogeneous nickel or palladium phosphine complexes (*e.g.*, $[NiCl_2(dppp)]$, where dppp $= Ph_2P(CH_2)_3PPh_2$). Recently Lipshutz has reported an example where nickel(II) nitrate immobilised on carbon has been used as a precursor catalyst in the reaction. However, this must first be chemically reduced in the reaction mixture to give the active Ni(0) form and this leads to a complex reaction cocktail with the possibility that side reactions may occur [4]. A range of polymer-supported catalysts are now appearing in the literature and have shown a variety of success in terms of their ability to promote solution phase reactions [5].

We have been investigating the immobilisation of non-symmetric transition metal co-ordination complexes based on N_2O_2 chelating ligands that can be covalently bound onto polymer and oligomer backbones using a single point of attachment on the ligand, thereby ensuring mobility of the complex [6]. Merrifield (chloromethylstyrene–divinylbenzene cross-linked co-polymer) resin [7] polymer beads, which possess active chloromethylstyryl groups, are commercially available and can be functionalised for use in combinatorial or high throughput chemistry. Here we report the use of a new non-symmetric nickel(II) catalyst covalently bound to a Merrifield resin through a single point of attachment as an efficient catalyst for the Tamao–Kumada–Corriu reaction.

2. Experimental and methods

Organic reagents were obtained from Aldrich or Lancaster Synthesis and used without further purification. Merrifield (chloromethylpolystyrene–divinylbenzene) resin beads (macroporous, 150–300 μm, 50–100 mesh, 2 mmol-Cl g^{-1}, 2% DVB cross-linker) were obtained from Polymer Labs. THF was distilled from sodium benzophenone prior to use and stored over 4A molecular sieve. Infrared spectra were recorded on a Perkin–Elmer 783 spectrometer. ^1H NMR spectra were recorded on a Jeol JNM-LA400 spectrometer operating at 400 MHz and chemical shifts are reported in parts per million with reference to internal $SiMe_4$. Elemental analysis was performed on a Fisons Instruments Carlo-Erba EA 1108 CHN analyser using acetanilide as the reference standard. V_2O_5 was added to aid combustion in the nickel complex as early analyses consistently reported low elemental percentages. Mass spectra were recorded on a Finnigan Mat 1020 GC-MS spectrometer (electron ionisation mode/70 eV). GC analysis was performed using a Chrompack CP9001 with a 10 m CP-SIL 5CB column and GC-MS using a Finnigan MAT GCQ with a 30 m Restek Rtx®-5MS column. In each case the temperature program

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was 60–300 °C at 20 °C min^{-1}, with an initial 1 min isothermal hold at 60 °C, and a final temperature isothermal hold of 6 min. The MS mass limit was set between 40 and 500 Da. Analysis by inductively coupled plasma-mass spectrometry (ICP-MS) was performed on a Fisons Instruments PlasmaQuad 40 emission ICP-MS.

2.1. *7-amino-5-aza-4-methyl-hept-3-en-2-one (**1**)*

A solution of pentan-2,4-dione (10.0 g, 0.10 mol) in DCM (250 ml) was cooled with stirring to 0 °C. A solution of 1,2-diaminoethane (6.0 g, 0.01 mol) in DCM (250 ml) was added and the solution allowed to stir for 2 h while being allowed to come to room temperature. The solvent was removed *in vacuo* to give crystals in an oil. Recrystallisation from n-pentane yielded colourless crystals. Yield = 7.1 g (50%) [8].

^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ_H 10.90 (s, 1H, NH), 5.00 (s, 1H, CH=), 3.40 (m, 4H, N–CH_2CH_2–N), 2.85 (t, 2H, NH_2), 1.95 (dt, 6H, CH_3).

IR (KBr): ν (cm^{-1}): 3369 (s), 1611 (s), 1445 (m), 1358 (m), 1296 (s), 1021 (w), 740 (w), 651 (w).

MS (m/z): 45, 54, 70 (100%), 82, 98, 112, 125, 142 $[M]^+$.

2.2. *[9-(2,4-dihydroxyphenyl)-5,8-diaza-4-methyl-non-2,3,8-trienato](2-) nickel(II) (**3**)*

2.2.1. *Method A*

A solution of **1** (1.0 g, 7 mmol) in DCM was stirred with cooling at 0 °C. A solution of 2,4-dihydroxybenzaldehyde (0.97 g, 7 mmol) in methanol (1 ml) and DCM (100 ml) was added and the solution stirred (10 min) and then allowed to come to room temperature. Repeated attempts using a variety of purification techniques failed to yield pure ligand so nickel acetate tetrahydrate (1.99 g, 8 mmol) was added and the solution was heated under reflux overnight. The red crystals that formed during the reaction were filtered off and air dried. Recrystallisation from methanol with a hot filtration yielded the product as red microcrystals. Yield = 0.16 g (7%). Mp = 208–210 °C.

2.2.2. *Method B*

A solution of 1,2-diaminoethane (0.5 g, 8.32 mmol) in DCM (10 ml) was added dropwise to a stirred solution of pentan-2,4-dione (0.83 g, 8.29 mmol) in DCM (10 ml) at room temperature. On complete addition, stirring was continued for a further 10 min. A solution of 2,4-dihydroxybenzaldehyde (1.15 g, 8.33 mmol) in methanol (1 ml) and DCM (9 ml) was added and the solution stirred (10 min). Nickel acetate tetrahydrate (1.69 g, 6.8 mmol) was then added and the solution was heated under reflux (30 min). The red crystals that formed during the reaction were filtered off and air-dried. Recrystallisation from methanol with a hot filtration yielded the product as deep red microcrystals. Yield = 1.48 g (68%). Mp = 208–210 °C.

^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ_H 9.70 (s, 1H, Ar–OH), 7.60 (s, 1H, Ar–H), 7.04 (d, 1H, Ar–H, J 9.5 Hz), 6.0 (m, 3H, overlapping Ar–H and CH=), 3.31 (m, 10H, CH_3 and N–CH_2).

Calculated for $C_{16}H_{20}N_2NiO_3$: C 52.71, H 5.06, N 8.78; found C 52.23, H 4.77, N 8.41.

IR (KBr): ν (cm^{-1}): 3158 (m), 1621 (s), 1543 (s), 1452 (m), 1233 (s), 1178 (w), 1131 (s), 986 (m), 844 (m), 790 (w), 663 (m), 569 (w), 465 (w), 439 (w).

MS (m/z): 77, 105, 123, 148, 169, 193, 207, 231, 247, 275, 303, 318 $[M–H]^+$ (100%).

2.3. *Resin-immobilised [9-(2,4-dihydroxyphenyl)-5,8-diaza-4-methyl-non-2,3,8-trienato] (2-)nickel(II) (**4**)*

A deep red solution of **3** (0.4 g, 1.25 mmol) in DMF (10 ml) and THF (5 ml) was added dropwise at room temperature to a dispersion of 60% sodium hydride in mineral oil (60 mg, 1.25 mmol) and the resulting solution stirred for 10 min. A suspension of the Merrifield resin (0.725 g, 2 mmol-Cl g^{-1}, 1.25 mmol-Cl) that had been pre-swelled in DMF (10 ml) for 30 min was then added and the mixture stirred gently at room temperature for 24 h. The initially white Merrifield resin beads became deep red in colour and the solution turned pale yellow/orange. The beads were filtered off through a course frit sinter using a diaphragm pump. The beads were washed with water (3 × 25 ml) and dichloromethane (3 × 25 ml) and air-dried. Yield = 0.81 g.

2.4. *ICP-MS analysis of the beads*

Calibration against nickel standards and a blank was linear. Weighed samples for ICP-MS were placed in Teflon vessels and digested slowly at room temperature into concentrated nitric acid (Romil SpA grade). The digest was then diluted to 10 ml with water. Analysis showed there to be 0.883 wt% nickel in the beads, corresponding to a complex loading of 15.0 $\mu\mathrm{mol\,g}^{-1}$ of resin. The original chloromethylstyrene beads showed zero nickel content as expected. Solutions from the catalytic runs using the nickel-functionalised resin likewise showed zero nickel content (at sub-ppb detection) which shows that nickel is not leaching from the beads over the course of a reaction.

2.5. *General procedure for the catalytic reactions*

A solution of an organobromide (0.5 mmol) in dry distilled THF (1 ml) was added to a Schlenk tube containing the catalyst resin **4** (0.5 mol%) and shaken for 1 min. The Grignard reagent (1 M in THF, 0.5 ml) was transferred *via* syringe needle under an atmosphere of nitrogen and added directly into the solution of organobromide and the reaction mixture was stirred magnetically. An inert atmosphere was not required in the reaction vessel itself. Aliquots were withdrawn at different time intervals and the samples quenched by addition to saturated aqueous sodium hydrogen carbonate. The organic components were extracted into ether, dried over magnesium sulfate and the resulting solution analysed by GC and GC-MS. The catalyst beads can be recovered by filtration and used repeatedly in further reactions without any noticeable degradation in catalytic activity (a single batch of beads has been used in a total of ten separate reactions over a period of time, see later).

2.6. Batch scale synthesis of 2-(4-methoxyphenyl)thiole (entry 12)

A solution of 4-bromoanisole (2.3 g, 12.3 mmol) in THF (20 ml) was added to the catalyst resin (100 mg, 1.5 μmol nickel complex, 12 mmol%) contained in a 100 ml three-necked round bottom flask under an atmosphere of dry nitrogen and stirred for 30 min in order to swell the resin. In a separate flame-dried flask, a solution of 2-bromothiole (2.0 g, 12.3 mmol) in THF (50 ml) was added over magnesium turnings (0.3 g, 12.3 mmol) under an atmosphere of dry nitrogen and the whole heated with rapid stirring until the magnesium had been consumed. The cooled solution was transferred to the three-necked flask *via* syringe through a rubber septum and stirring continued at room temperature. Samples were withdrawn at regular intervals and analysed by GC. After 19 h the reaction was quenched by adding saturated aqueous sodium hydrogen carbonate and the crude product extracted into ether. GC analysis indicated 71% conversion based on 4-bromoanisole. The product was isolated as pale green-yellow crystals by flash chromatography on silica gel using 5% ethyl acetate in hexane as the eluent. Yield = 1.38 g (59%). Mp = 104.5–105 °C (lit. 105–106 °C) [9].

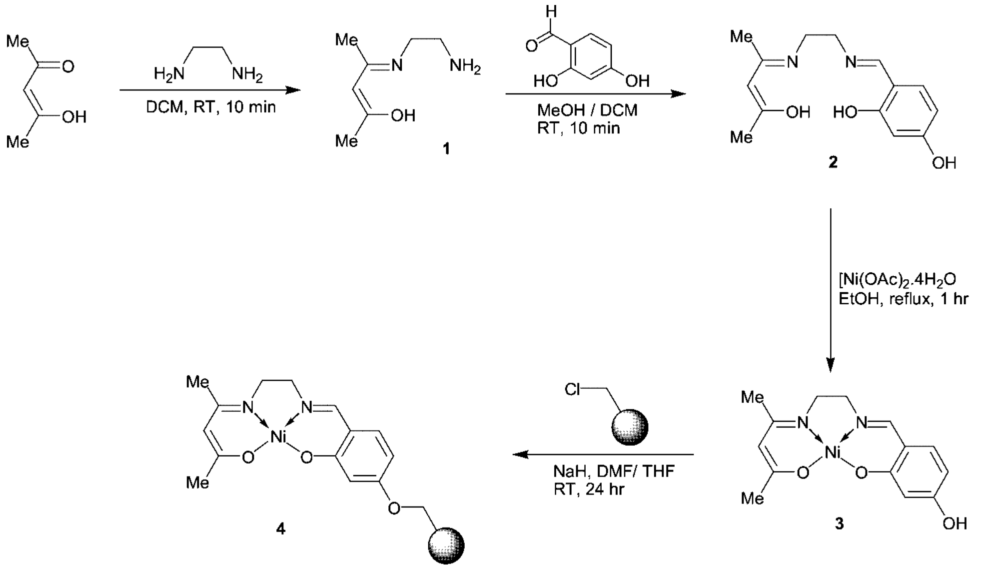
^{1}H NMR ($CDCl_3$): δ_H 7.35 (2H, AA$'$XX$'$, J 7.5 Hz, phenyl 2-H); 7.21 (1H, AB, J 4.5 Hz, thiole 5-H); 7.17 (1H, AB, J 4.0 Hz thiole 3-H); 7.15 (1H, ABX multiplet, thiole 4-H); 6.78 (2H, AA$'$XX$'$, J 7.5 Hz, phenyl 3-H); 3.78 (3H, s, CH_3O).

3. Results and discussion

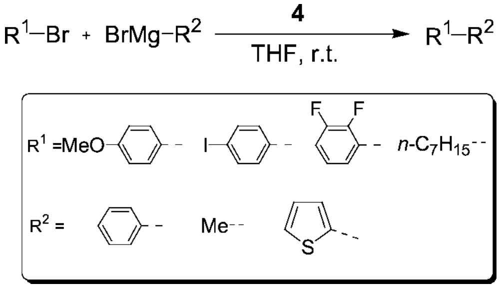
Unsymmetrical salen-type complexes were synthesised using a one-pot method that allowed the yield to be optimised. The salen-type complexes were targeted because of their simple structures with single points of attachment, making synthesis relatively straightforward, and their low cost. A solution of 1,2-diaminoethane in dichloromethane was added dropwise to an equimolar solution of pentan-2,4-pentandione also in dichloromethane and rapid stirring was continued for 10 min at room temperature (scheme 1). A solution of 2,4-dihydroxybenzaldehyde in dichloromethane/methanol was then added and stirring continued for a further 10 min at room temperature. A solution of nickel(II) acetate tetrahydrate in methanol was added to the reaction solution and the whole was refluxed for 1 h with rapid stirring. The target complex (**3**) precipitated as a red powder during the course of the reaction and was recovered by filtration. Analytically pure **3** was obtained by recrystallisation from hot methanol as red microcrystals in a yield of 68%.

The complex was attached to a macroporous Merrifield resin (Polymer Labs, 2 mmol-Cl g^{-1}, 150–300 μm, 50–100 mesh, 2% DVB cross-linker) by taking advantage of the acidic phenolic proton located outside the chelation motif of the ligand. A solution of **3** in DMF/THF was added dropwise at room temperature to a dispersion of 60% sodium hydride in mineral oil and the resulting solution stirred for 10 min. A suspension of the Merrifield resin that had been preswelled in DMF for 10 min was then added and the mixture stirred gently, to avoid mechanical damage, at room temperature for 24 h. The initially white Merrifield resin beads became deep red in colour and were isolated by filtration.

The intractable nature of the complex-coated beads (**4**) meant that it was not possible to characterise them by conventional spectroscopic techniques. However, inductively coupled plasma-mass spectroscopy (ICP-MS) was performed on the native Merrifield resin and on the immobilized complex [8]. Quantitative analysis relative to a standard solutions containing 0, 10, 25 and 50 ppm nickel showed the native resin to contain no nickel, as expected, and the complex-immobilised beads to contain 8.83 ppm

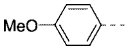
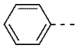
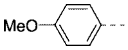
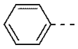
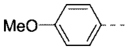
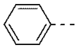
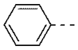
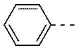
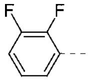
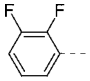
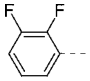
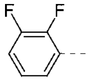
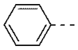
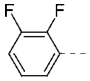
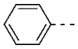
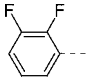
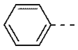
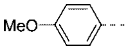
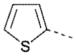


Scheme 1. Synthesis of the catalyst complex and its immobilisation on a Merrifield resin.



Scheme 2. General procedure for the catalyst studies.

Table 1
Reaction times and GC yields from the catalyst studies.

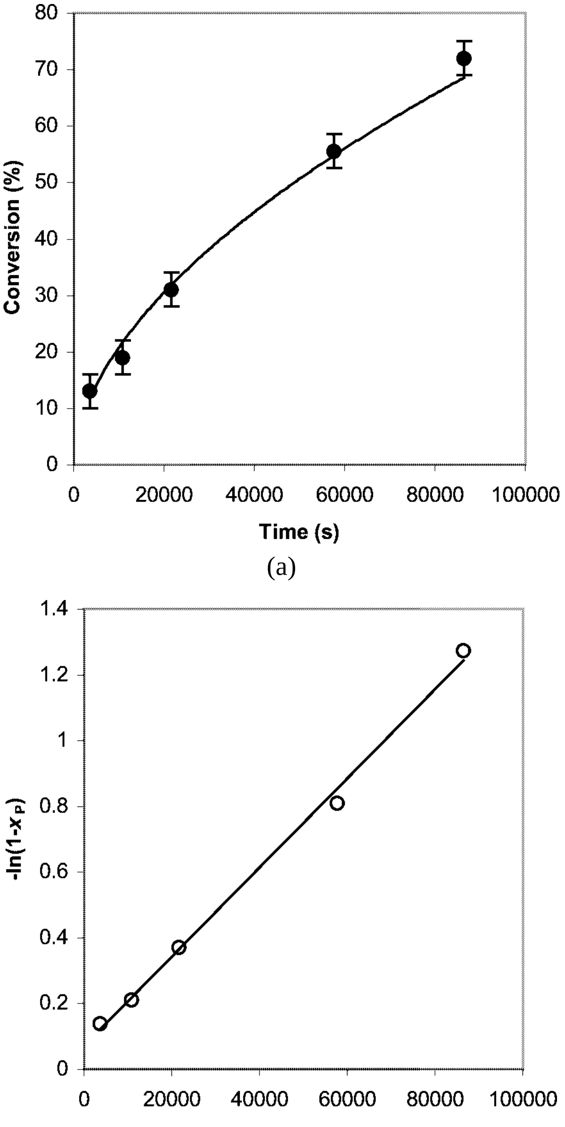
Entry	R^1	R^2	Molar ratio R^2MgBr/R^1Br	Time	Yield (%)
1			1	1 h	11–14
2			1	16 h	54–57
3			1	24 h	71–73
4			1	5 min	40–42
5	n-C_7H_{15}--		1	16 h	37–42
6		CH_3--	1.5	5 min	72–74
7		CH_3--	1.5	16 h	72–75
8		CH_3--	3	5 min	>99
9			3	5 min	12–16
10			3	5 h	29–32
11			3	16 h	86–88
12			1	19 h	71

nickel, representing 0.883 wt%. Relative to the chlorine content on the native resin, this represents an 11.8% loading of the beads or 15.0 μmol catalyst per gram of resin. The intractable nature of the beads and the low loading of catalyst made it impossible to obtain meaningful data from infrared analysis. Attempts to obtain spectra by ATR methods or by grinding with KBr were unsuccessful and the spectrum of the complex on the bead was masked by the bulk of the polymer support. Therefore, proof that the nickel complex is immobilised covalently to the resin comes from the ICP-MS data of the beads and analysis of the reaction solutions, which show no leeching of the metal into solution.

The catalyst was tested at room temperature against a range of substrates (scheme 2) in the Tamao–Kumada–Corriu reaction (table 1). In a typical catalytic run, 0.5 mmol of an organobromide in 1 ml dry distilled THF was added to a Schlenk tube containing the catalyst resin **4** (0.5 mol%) and shaken for 1 min. The Grignard reagent (1 M in THF, 0.5 ml) was transferred *via* syringe needle under an atmosphere of nitrogen and added directly into the solution of organobromide and the reaction mixture was stirred magnetically. The resulting solution was analysed by GC and GC-MS. The catalyst beads can be recovered and used indefinitely in further reactions without any degradation in catalytic activity. ICP-MS analysis of the crude reaction mixtures after reaction revealed no nickel in the solution phase, thereby proving that the metal was not leaching from the catalyst. Each reaction is summarised in table 1, which gives the range of GC yields over three runs using the same beads in each case with a single run for entry 12.

Entries 1–3 in table 1 show the reaction of phenylmagnesium bromide with 4-bromoanisole to give 4-methoxybiphenyl. While no reaction was observed in the absence of the catalyst or in the presence of the unfunctionalised Merrifield resin, 11–14% conversion to the expected product (m/z = 184 Da) was observed after 1 h stirring. When the reaction was left for 16 h, the yield had improved to 54–57% and 71–73% after 24 h, which is comparable to yields observed in the related Suzuki coupling at elevated temperatures. The reaction is therefore assumed to be first order overall, as indicated by the reaction profile in figure 1(a), and integration leads to the observed rate constant (k_{obs}) of 2×10^{-5} s^{-1} from the slope of the graph in figure 1(b). The fact that this reaction proceeds at room temperature is therefore advantageous, as no external heating or cooling sources are required. The reaction solution at the end of the first run was reduced to dryness and the residue analysed by ICP-MS. This showed a zero reading for nickel even at sub-ppb sensitivities. Therefore, there is no doubt that the metal remains bound to the resin throughout the catalytic cycle. This is in contrast to heterogeneous catalysts where the metal species such as palladium(II) acetate is absorbed onto a solid support such as carbon or silica. It has been shown by Schmidt *et al.* that in such cases the palladium leaches from the support over the course of a reaction and that catalysis continues in solution after the support is removed by filtration [10]. Indeed, homogeneous palladium is detected in reaction solutions by atomic absorption spectroscopy in up to 50% of the initial metal content on the support. This is clearly not the case in the immobilised nickel catalyst reported here as reaction solutions have been shown to be nickel-free.

In order to test the efficiency of the catalyst over repeated reaction cycles, the same reaction was repeated a total of ten times over a period of two months, the original catalyst resin being filtered off, stored and re-used in each reaction. Reactions were stirred for 24 h at room temperature without monitoring the detailed kinetics. In each case the GC yield of 4-methoxybiphenyl was approximately constant (±5%) ranging from 62 to 72% with a mean value of 67.5%. Fur-



(a)

(b)

Figure 1. Kinetic data obtained from the reaction of 4-bromoanisole with phenylmagnesium bromide over 19 h. A rate constant of 2×10^{-5} s^{-1} is obtained assuming the process to be first order overall in terms of the organobromide.

thermore, the yield was independent of run order with some of the higher yields being observed after the catalyst had been re-used several times.

Entry 4 shows the reaction of phenylmagnesium bromide with 4-bromoiodobenzene. The major product from the reaction is 4-iodobiphenyl ($m/z = 280$ Da) in a yield of 40–42% after 16 h. This is unusual as the major product in the Suzuki coupling (using phenylboronic acid and 4-bromoiodobenzene) is 4-bromobiphenyl ($m/z = 232/234$ Da), which was observed here in only a 10% yield. Therefore, the catalyst is showing an unexpected selectivity for the replacement of the bromo rather than the iodo substituent. Entry 5 shows the versatility of the catalyst for direct alkylation of a benzene ring using phenylmagnesium bromide and n-bromoheptane to give n-heptylbenzene ($m/z = 176$ Da). Despite the yield of only 37–42%, this is in fact a significant improvement over conventional methods that typically require four steps [11], involving cryogenic temperatures and a catalytic hydrogenation, taking several days to complete and with an overall yield of only 30%.

Entries 6 to 8 describe the reaction of methylmagnesium bromide with 3-bromo-1,2-difluorobenzene. Because the by-product of the quenching reaction in this case is methane, an excess of the Grignard reagent was used in each case. In entry 6 a 1.5 molar excess of the Grignard reagent was used and was found to give the desired product, 2,3-difluorotoluene ($m/z = 128$ Da) in 72–75% yield in less than 5 min at room temperature. Extending the reaction time to 16 h (entry 7) showed no improvement in the yield. If a three-fold excess of the Grignard reagent was used the yield was found to be in excess of 99% in under 5 min with the GC chromatogram showing only a trace of starting material that did not integrate. The reaction of a three-fold excess of phenylmagnesium bromide with 3-bromo-1,2-difluorobenzene at room temperature produced 2,3-difluorobiphenyl ($m/z = 190$ Da) in only 12–16% in 5 min. When the reaction time was increased to 5 h the product yield increased to 29–32% (entry 10). When the reaction was left overnight (entry 11) the conversion of the bromide to the product increased to 86–88%. Analysis of this data also shows the overall reaction to be first order in the bromide giving the observed rate constant (k_{obs}) as 3×10^{-5} s^{-1}, which is comparable with the case described for the reaction of 4-bromoanisole with phenylmagnesium bromide.

Entry 12 shows the reaction of 4-bromoanisole with thiophenylmagnesium bromide to yield 2-(4-methoxyphenyl) thiole. In order to test the viability of the immobilised catalysts in larger batch scale processes, the reaction was scaled-up to a realistic preparative level. The Grignard reagent was prepared from 2-bromothiole and used directly in the coupling reaction. Reaction was carried out over 19 h to yield 71% of the target product by GC analysis. This gives a turnover number of 5800 for the given conditions. The conditions here were not optimised so we are undertaking further studies to determine the maximum turnover number for the system. The whole solution was quenched with saturated aqueous sodium hydrogen carbonate and the bright green aqueous solution extracted into ether. Separation of the crude reaction mixture by flash chromatography yielded the target material as a pale green-yellow solid in 59% yield. While the same material has been prepared in slightly higher yield by other processes, these typically include organo tin [12] (Stille), lead [13], copper [9] (Ullman) or tellurium [14] reagents under much harsher and less environmentally friendly conditions and using homogeneous catalysis. For example, the Ullman reaction requires the use of n-butyllithium at 0 °C followed by conversion to the organocopper reagent and 8 h reaction at 150 °C. In the example reported here, the reaction uses the readily formed Grignard reagent with an organobromide at room tempera-

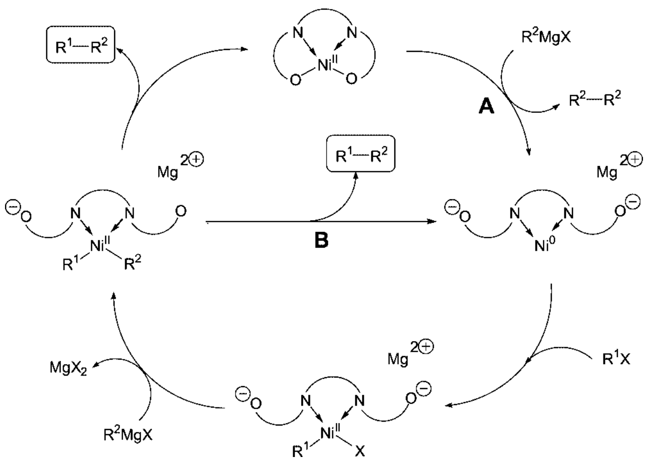


Figure 2. Proposed catalytic cycle for the Tamao–Kumada–Corriu reaction using the immobilised nickel catalyst, showing the initial sacrifice of Grignard reagent (**A**) to give zero-valent nickel. The hard anionic oxygen donors are charge balanced by the magnesium ion and the nickel remains coordinated due to the presence of the soft nitrogen donor atoms.

ture. Therefore, we have demonstrated this to be a green synthetic approach as the conditions are not so harsh, free from toxic metal reagents and the immobilised nickel catalyst is readily recovered.

The mechanism of catalysis is under further investigation, however a proposed catalytic cycle is shown in figure 2. The results from ICP-MS show without doubt that the nickel is retained on the resin even after numerous reactions and on prolonged exposure to both solvents and substrates. Furthermore, one of the reaction by-products when using phenylmagnesium bromide is biphenyl and this gives some information pertinent to the mechanism. The possibility of two competing cycles exists. The complex in the free and immobilised form possesses a hard central Ni^{2+} ion chelated by both hard (anionic oxygen) and soft (neutral nitrogen) donor atoms from the ligand. Route **A** involves pre-activation of the catalyst by reduction to Ni(0), chelated by soft nitrogen donors, with the production of the homocoupled organic product through sacrifice of some of the Grignard reagent. Homocoupled product was identified in each case (in typically <20% conversion) for phenylmagnesium bromide (biphenyl) but was not isolated in the case of methylmagnesium bromide (ethane) because of the volatility of the product. This is an essential step as Ni^{2+} is inactive towards the oxidative addition of the organobromide. However, in general the yield of homocoupled product is not proportional to the main coupling product so the possibility arises that the catalyst takes an alternative pathway (route **B**) once catalyst initiation has occurred. As substantially more heterocoupled product is observed, it is proposed that the rate constant for route **A** is smaller than for route **B**. We are currently investigating the kinetics of the reaction in order to elucidate the exact reaction pathway using both time-dependent GC and *in situ* NMR analysis of the reaction mixtures.

4. Conclusions

In summary, the procedure described represents a useful method for the room temperature formation of carbon–carbon bonds using both sp^2 and sp^3 hybridised carbon substrates. The nature of the immobilised catalyst means that it is easily prepared, recovered and recycled and is therefore extremely cost effective. Furthermore, the supported catalyst lends itself to high throughput solution phase chemistry, in particular in the production of pharmaceuticals and fine chemicals because the products are free from transition metal contamination. The rapid reaction times for some of the substrates means a large number of materials may be screened in parallel [15] over a short time period. We have also shown that the catalytic reaction can be scaled-up to produce useful synthetic quantities of target compounds, without the use of toxic metal reagents. Therefore, this represents a “green” process that should have advantages for industry.

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