This article is published as part of the Dalton Transactions themed issue entitled:

Pincers and other hemilabile ligands

Guest Editors Dr Bert Klein Gebbink and Gerard van Koten

Published in issue 35, 2011 of Dalton Transactions



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Dalton **Transactions**

Cite this: Dalton Trans., 2011, 40, 8935

PAPER

Iron(II) complexes with functionalized amine-pyrazolyl tripodal ligands in the cross-coupling of aryl Grignard with alkyl halides[†]

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Received 16th February 2011, Accepted 24th March 2011 DOI: 10.1039/c1dt10258c

Structurally distinctive Fe(II) complexes with furan, thiophene and pyridine functionalized amine-pyrazolyl tripodal hybrid ligands have been synthesized and crystallographically characterized. The tether substituent at the central amine plays an active role in determining the coordination mode of the ligand and the metal geometry. All complexes are catalytically active towards cross-coupling of aryl Grignard reagents with primary and secondary alkyl halides with β-hydrogen under ambient conditions, ESI-MS spectra analysis revealed the ligand-stabilised Fe(II) and Mg(II) species.

Introduction

Use of iron in catalytic reactions is of topical significance in view of the abundance of iron and its relatively low toxicity.¹ Among the many reactions of interest, the cross-coupling of primary and secondary alkyl halides with aryl Grignard reagents is noteworthy due to their high cross-coupling selectivity with minimum β -elimination by-products, the latter of which still plague many nickel- and palladium-catalysed systems.1a,2-6 Some common iron compounds have been proven to be active toward such cross coupling. For example, in the presence of excess of an amine additive, such as TMEDA (N,N,N',N'-tetramethylethylenediamine), FeCl₃^{3a} and Fe(acac)₃ $(acac = acetylacetonate)^{3b}$ are active towards the cross-coupling of aryl Grignard reagents with secondary bromides or chlorides. The preparative simplicity offers another advantage of the use of iron complexes in catalysis. For example, some amine, phosphine, arsine and N-heterocyclic carbene complexes of iron formed in situ from iron chlorides (mainly anhydrous FeCl₃) could give up to 90% of the cross coupling product of bromocyclohexane with p-tolymagnesium bromide.⁴ Structurally defined complexes have also been applied, such as $[Fe^{III}Cl_3L]$ (L = 1,3,5trimethylhexahydro-1,3,5-triazine),^{4a} [Fe^{II}(IPr)Br₃](HIPr)₃·C₇H₈ (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene),^{5a} ionic liquid $[bmim][Fe^{III}Cl_4]$ (bmim = butylmethyl imidazolium),^{5b} [Fe^{III}ClL] (L = amine-bis(phenolate)ether)^{5c} and [Fe^{III}Cl(salen)]^{5d} The discrete molecular complex [(Fe^{III}Cl₃)₂(tmeda)₃] also shows

some advantages over the in situ mixtures of FeCl₃/TMEDA system.^{3b} Low-valent iron complexes, [Li(tmeda)]₂[Fe^{-II}(C₂H₄)₄] is effective towards the coupling of a large range of alkyl halides with diverse functionalities.2e,6

Encouraged by the promotional effect of amines, notably TMEDA, in these reactions and the recent discovery that $Fe^{II}Ar_2$ (tmeda) and $Fe^{II}ArBr$ (tmeda) (Ar = aryl) are possible intermediates in the FeCl₃/TMEDA catalyzed coupling reactions of ArMgX with alkylbromides,^{2f} we are interested to apply some easy-to-prepare, air-stable and structurally distinctive Fe(II) complexes to aryl Grignard cross-couplings with alkyl halides with β -hydrogen. In line with our current interest in hybrid ligands tethered by dissociable ligands with enhanced hemilabile functions,7-9 the ligands of interest here are amine-pyrazolyl derivatised by a pendant function. Apart from the structural and catalytic findings, we also report the ESI-MS species of the catalytic mixtures which could shed some light on the active species involved.

Results and discussions

Synthesis and characterization of Fe(II) complexes 1-4

Four furan, thiophene and pyridine functionalized aminepyrazolyl tripodal ligands L₁-L₄ have been prepared from the reactions between (3,5-dimethyl-1H-pyrazol-1-yl)methanol and the corresponding amine based on adapted literature methods.¹⁰ They are characterized by NMR, ESI-MS spectroscopic analyses and elemental analysis.

L1-L4 complex readily to FeCl2·4H2O in THF giving the corresponding Fe(II) complexes 1-4 in good yields (Scheme 1). All four complexes give the characteristic molecular ion peaks of [FeClL]⁺ in the positive mode of ESI-MS spectra. Diffusion of Et_2O into the complex solutions in CH_2Cl_2 at r.t. afforded yellow single crystals of 1, 3 and 4 suitable for X-ray crystallographic analysis.

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Molecular structure of compounds 1, 3 and 4 determined by single-crystal X-ray diffraction

Although all three (1, 3 & 4) are Fe(II) complexes, they show distinctly different metal geometries influenced by the tripodal ligands with hemilabile function.

Complex 1 is (distorted) tetrahedral with bidentate chelating coordination of L_1 through the nitrogen atoms of pyrazolyl rings (Fig. 1). The central amine is notably non-coordinating thus giving an 8-membered metallocyclic ring. The furan arm is understandably pendant. Similar structure has been found in the Fe(II) bis(2-oxazolin-2,5,5-trimethyl)phenylphosphine complexes with the ligand in a N,N coordination mode.¹¹



Fig. 1 ORTEP diagram of 1 (30% probability ellipsoids). Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): Fe1–N1 2.0856(18), Fe1–N3 2.1038(19), Fe1 \cdots N5 3.979(2), Fe1–Cl1 2.2486(7), Fe1–Cl2 2.2663(7). N1–Fe1–N3 108.75(7), N1–Fe1–Cl1 100.46(5), N1–Fe1–Cl2 111.57(5), N3–Fe1–Cl1 116.46(6), N3–Fe1–Cl2 101.16(5), Cl1–Fe1–Cl2 118.51(3).

Change in the pendant function and adjustment in the spacer between the pendant and the central amine nitrogen impart a significant difference on the coordination motif of the ligand and metal geometry. This is witnessed in the tridentate coordination of amine-pyrazolyl ligand and trigonal bipyramidal Fe(II) in **3** (Fig. 2) and tetradentate coordination of the pyridyl-amine-pyrazolyl ligand and octahedral Fe(II) in **4** (Fig. 3).



Fig. 2 ORTEP diagram of 3 (30% probability ellipsoids). Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): Fe1–N1 2.1185(17), Fe1–N3 2.1209(16), Fe1–N5 2.4064(15), Fe1–Cl1 2.3086(6), Fe1–Cl2 2.3747(6). N1–Fe1–N3 113.18(6), N1–Fe1–Cl1 110.67(5), N1–Fe1–Cl2 103.68(4), N1–Fe1–N5 73.24(6), N3–Fe1–Cl1 126.02(5), N3–Fe1–Cl2 92.29(4), N3–Fe1–N5 72.43(6), N5–Fe1–Cl1 92.12(4), N5–Fe1–Cl2 160.87(4), Cl1–Fe1–Cl2 106.40(2).



Fig. 3 ORTEP diagram of 4(30% probability ellipsoids). Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (°):Fe1–N1 2.219(3), Fe1–N3 2.338(5), Fe1–N4 2.209(5), Fe1–Cl1 2.3512(16), Fe1–Cl2 2.4190(15). N1–Fe1–N3 74.29(8), N1–Fe1–N4 84.39(9), N1–Fe1–N1A 148.43(16), N1–Fe1–Cl1 105.16(8), N1–Fe1–Cl2 92.18(9), N3–Fe1–N4 74.6(2), N3–Fe1–Cl1 169.65(14), N3–Fe1–Cl2 92.38(14), N4–Fe1–Cl1 95.03(14), N4–Fe1–Cl2 166.99(13), Cl1–Fe1–Cl2 97.98(6).

In 3, although the pendant (thiophene) remains noncoordinative, the slight lengthening (by a methylene) of the spacer between the central amine nitrogen and the heterocyclic substituent is sufficient to push the amine nitrogen from nonbonding in 1 (Fe1...N5 3.979(2) Å) to within bonding distance with the metal in 3 (Fe1–N5 2.4064(15) Å), thus bisecting the 8-membered ring into two 5-membered rings. The latter Fe1–N5 bond is however significantly longer, and presumably weaker, than the coordination of the pyrazolyl ring Fe1–N1 and Fe1–N3 of 2.1185(17) and 2.1209(16) Å, respectively. This structure is similar to some compounds formed between FeCl₂ and α -substituted tris(2-pyridylmethyl)amine (TPA) ligands,¹² for example, FeCl₂(R₂TPA) (R = Br, Ph) in which the tripod is tridentate with a substituted pyridyl arm being pendant. The sharp increase of iron-amine contact from 1 to 3 exemplifies the hemilability nature of this type of hybrid ligand which adds the skeletal flexibility to the resultant metallomacrocyclic ring. Such coordination and conformational freedom allows the metal to adjust its geometry to adapt to the environmental change, which is an important attribute in a catalytic metal moiety.

The ligand-initiated geometric change is substantiated in 4 when a more basic pyridyl substituent is introduced to the amine. As expected, all the functional groups (pyrazolyl, amine & pyridyl) are coordinated, thus giving a tetradentate ligand binding to the metal with three orthogonal 5-membered metallomacrocyclic rings. Significantly, the pyridyl coordination has further shortened the iron-amine bonding contact to Fe1-N3 2.338(5) Å (from Fe1-N5 2.4064(15) Å in 3). This formation provides crystallographic evidence that a functional tether at the center of a tripodal ligand could influence not only the coordination mode of the ligand but also the strength of its central anchor. The Fe-Cl lengths understandably increase as the coordination number increases from 1 (Fe–Cl_{ave}. = 2.258 Å) to 3 (Fe–Cl_{ave}. = 2.342 Å) to 4 (Fe– $Cl_{ave} = 2.385$ Å). Pyridyl coordination in **4** weakens the *trans* Fe1– Cl2 to 2.4190(15) Å, which is the longest in this series, suggesting that it may be possible to use the tether effect to labilise the Fe-Cl bond to achieve metal activation in catalysis.

Cross-coupling of aryl Grignard reagents with alkyl halides

Iron-catalysed cross-coupling reactions of aryl Grignard reagents with primary or secondary alkyl halides with β -hydrogen are mostly conducted on Fe(III) complexes²⁻⁵ Recently, Sun *et al.*^{5a} reported a highly active anionic iron(II) NHC complex towards cross-coupling of *p*-tolylmagnesium bromide with bromocyclohexane. Little is known on the use of heterocycle-based hybrid ligands in Fe(II) complexes in this type of catalysis. We are interested in applying the structurally characterized complexes **1–4** and examine if the tether-imposed structural features could have any influence on the catalytic activities.

Initial screening was carried out on the r.t. reaction of bromocyclohexane (A) with PhMgBr as a representation of aryl Grignard– secondary alkyl coupling catalysed by 1-4 (Scheme 2), with FeCl₂ and FeCl₂·4H₂O included for comparison (Table 1).



In the absence of catalyst, only trace amount of homo-coupled product, biphenyl, was detected (GC-MS). The ligand L_1-L_4 without metal show no activity. All complexes (1–4) at 5 mol% at r.t. show high yields of cyclohexylbenzen (**B**). These activities are comparable or better than those reported molecular systems.⁵ The differences in this series are not significant but among them, **4** is most effective, with quantitative conversion and yield whereas **2**, with a thiophene pendant connected through a short

 Table 1
 Catalytic activity of Fe(II) compounds on the coupling of PhMgBr with bromocyclohexane^a

| Catalyst (5 mol% Fe) | Yield ^{b} of B (%) | Conversion ^{b} of A (%) | |
|---|---|---|--|
| FeCl ₂ | 33 | 54 | |
| FeCl, 4H,O | 88/41 ^c | 100 | |
| FeCl ₂ ·4H ₂ O/L4 | 96 | 100 | |
| 1 | 96 | 100 | |
| 2 | 85 | 100 | |
| 3 | 95 | 100 | |
| 4 | 99/85 ^d /62 ^e | 100 | |

^{*a*} Conditions: bromocyclohexane (1.0 mmol), PhMgBr (2.0 mmol), catalyst (5 mol%), THF, r.t., 40 min; ArMgBr was added dropwise for 30 min. ^{*b*} Yield and conversion are determined by ¹H NMR (mesitylene as internal standard). ^{*c*} bromocycloheptane was used as substrate. ^{*d*} 1 mol% Fe. ^{*e*} ArMgBr was added in one portion.

methylene spacer, gives the lowest yield of **B** (85%). The pendant effect is marginal, similar to those found in some Fe(III) aminebis(phenolate) complexes.^{5d} FeCl₂ is active but not effective whilst FeCl₂·4H₂O has a similar effect to **2**. However, the yield of **B** increases (from 88 to 96%) when L₄ is added stoichiometrically to FeCl₂·4H₂O, which suggests clearly the promoting effect of the ligand. It also suggests that the present system does not require the presence of ligand in excess to achieve high catalytic activities. The ligand effect is also witnessed when **4** gives better yield (76%) (Table 2, entry 2) than FeCl₂·4H₂O (41% yield) when bromocycloheptane is used as the substrate.

When the catalyst load is reduced to 1 mol%, otherwise under similar conditions, **4** maintains its high conversion, but slightly lower selectivity towards the cross coupling product **B** (Table 1). Similar to some other iron catalysts, 2f,3a a slow addition of the Grignard substrate would ensure higher selectivity of the cross coupling product.

These results suggest that the octahedral complex 4 performs the best and hence it was examined further for the coupling between other primary or secondary alkyl halides and different aromatic Grignard substrates (viz. PhMgBr, p-TolMgBr & p-FC₆H₄MgBr (Tol = tolyl; FC₆H₄ = fluorophenyl)) in THF under similar conditions (Table 2). The catalyst load was kept at 5 mol% Fe for direct comparison. In general, bromocyclopentane and bromocycloheptane give higher cross-coupling yields than the open chain secondary alkyl bromides (comparing entries 1-2 with entries 3-4; entries13-15 with entry 16). (Bromomethyl)benzene is moderately active with PhMgBr, similar to those catalysed by Fe(III) amine-bis(phenolate),^{5d} but could achieve higher yield at lower temperature (-10 °C) (entry 7). Electron-rich p-TolMgBr shows similar activities (entries 13-17) as PhMgBr. Although chlorocyclohexane generally couples poorly with Grignard reagents,3b,4a,5c its current reactions with PhMgBr and p-TolMgBr give quantitative conversions with satisfactory yields (82% and 83%, respectively) at 45 °C (entries 6 and 17), which are similar to the Fe^{III}Cl(salen)-catalyzed reactions.⁴ Primary alkyl halides are also reactive with these Grignard reagents at elevated temperature (45 °C) (entries 9–12, 17–21 and 25–26), with the chain length showing little effect on the catalytic activity. Catalyst 4 is also tolerant of p-FC₆H₄MgBr with bromocyclohexane, giving rise to near-quantitative yield of the desired coupling product (entry 22). In contrast, Nakamura^{3a} and Fürstner^{6c} observed moderate activities in their systems when the electron-poor Grignard

 Table 2
 Cross-coupling of ArMgBr with alkyl halides using 4 as catalyst^a

| Entry | ArMgBr | Alkyl halide | Product | Yield% ^b |
|-------|--------|----------------------|--|------------------------|
| 1 | ✓—MgBr | bromocyclopentane | $\bigcirc \longrightarrow \bigcirc$ | 88/78 ^c |
| 2 | | bromocycloheptane | | 76 |
| 3 | | 3-bromopentane | $\bigcirc - \sub$ | 62 |
| 4 | | 2-bromopropane | $\overline{}$ | 65 |
| 5 | | 2-iodopropane | $\mathbf{k} = \mathbf{k} + \mathbf{k}$ | 69 |
| 6 | | chlorocyclohexane | | 35/82° |
| 7 | | (bromomethyl)benzene | | 46/70 ^d |
| 8 | | 1-iodobutane | $\bigcirc \frown \frown$ | 79 |
| 9 | | 1-bromobutane | $\bigcirc \frown \frown$ | 63 ^c |
| 10 | | 1-bromooctane | C ()6 | 57/72° |
| 11 | | 1-bromodecane | C Ys | 76 ^c |
| 12 | | 1-bromododecane | 10 ⁽¹⁾ | 61 ^{<i>c</i>} |
| 13 | — MgBr | bromocyclohexane | | 99 |
| 14 | | bromocyclopentane | | 79 |
| 15 | | bromocycloheptane | | 77 |
| 16 | | 3-bromopentane | | 72 |
| 17 | | chlorocyclohexane | | 83 ^c |
| 18 | | 1-bromobutane | | 61 ^{<i>c</i>} |
| 19 | | 1-bromooctane | ₩ ⁶ | 66 ^c |
| 20 | | 1-bromodecane | K K K K K K K K K K K K K K K K K K K | 73 ^c |
| 21 | | 1-bromododecane | 10 H | 67 ^c |
| 22 | F | bromocyclohexane | F | 98 |
| 23 | | bromocyclopentane | F- | 85 |
| | | | | |

| Table 2 | (Contd) |
|---------|---------|
|---------|---------|

| Entry ArMgBr | Alkyl halide | Product | Yield% ^b |
|--------------|-------------------|---------|---------------------|
| 24 | bromocycloheptane | F- | 60 |
| 25 | 1-bromooctane | F F | 84 ^c |
| 26 | 1-bromodecane | F F | 85 ^c |

^{*a*} Conditions: alkyl halide (1.0 mmol), ArMgBr (2.0 mmol), catalyst (5 mol%), THF, r.t., 40 min. ^{*b*} Yield of the cross coupling products and the conversion of alkyl halide are determined by ¹H NMR (mesitylene as internal standard). The conversion of alkyl halide for all reactions is 100% after 40 min except in Entry 6 which is 65% for the r.t. reaction. ^{*c*} 45 °C. ^{*d*}-10 °C.

reagent is coupled with bromocyclohexane. The reactions of p-FC₆H₄MgBr with different alkyl bromides also lead to the desired products in high yield (entries 23–26).

Compound 4 can be reused several times; the conversion of bromocyclohexane maintains 100% both for the 2nd and 3rd runs but the yields of **B** (see Scheme 2) lower to 75% and 66%, respectively. The loss of yield may be traced to the presence of excess Grignard reagent in the reaction system after the 1st and the 2nd runs. The +ve mode ESI-MS spectrum of the catalytic reaction mixtures using 3 as the catalyst upon 10 min of reaction gives a major peak of $[MgBrL_3]^+$ (448 m/z (75%)) and a minor peak of $[FeBrL_3]^+$ (478 m/z (17%)). For the mixture with 4 as catalyst, [MgBrL₄]⁺ (427 m/z (63%)) and [FeBrL₄]⁺ (459 m/z (100%)) are also observed. Their parent species could be the arylhalo intermediates [MgArBrL] and [FeArBrL] as proposed by Nagashima et al.2f The benefit of the hybrid ligands is exemplified in their complexation and hence stabilization of not only the Fe(II) catalysts but also the Grignard reagents, which could explain the good catalytic performance of this system.

Experimental

All preparations and manipulations were performed using standard Schlenk techniques under a nitrogen atmosphere. Solvents were dried by standard procedures. FeCl₂·4H₂O (99.99%, trace metal based) was purchased from Sigma-Aldrich. Elemental analyses for C, H, and N were performed on a Perkin-Elmer PE 2400 CHNS elemental analyzer. The ligands are chemically pure but isolated as oils which are susceptible to solvent occlusion, thus leading to imperfection in some analytical data. ¹H and ¹³C NMR analyses were measured in CDCl₃ with an AMX500 500 MHz FT NMR spectrometers. IR spectra were recorded on a Shimadzu IR-470 spectrometer using KBr pellets as IR matrix. GC-MS analyses were recorded on Agilent 6890N/5973N system. ESI-MS was performed on a Finnigan LCQ quadrapole ion trap mass spectrometer. Sample was introduced into the ESI-source using a syringe pump. The following ESI-MS parameters were kept constant for all measurement: Spray voltage = \pm 4.5 kV; Capillary T = 200 °C; Flow rate = 5 µL min⁻¹; Tube lens offset = 35 V and capillary voltage = 35 V. The spectra were obtained as an average of at least 20 scans.

Synthesis of ligand L1-L4

Ligands L_1 - L_4 were prepared by a common procedure as follows: The mixture of (3,5-dimethyl-1*H*-pyrazol-1-yl)methanol (1.26 g, 10 mmol) and 5 mmol of the corresponding amine (furfurylamine, 0.435 g; 2-thiophenemethylamine, 0.566 g; 2-thiopheneethylamine, 0.636 g; 2-picolylamine, 0.504 g) in MeCN (20 mL) was stirred in a closed vessel at r.t. for ~5d. The solvent MeCN was removed under reduced pressure. The resulted oil was re-dissolved in Et₂O (20 mL). The solution was washed by water (3 \times 15 ml). The ether layer was dried by anhydrous Na₂SO₄. After filtration, the solvent was removed on a rotatory evaporator. The product was obtained as pale yellow oil. For bis[(3,5-dimethyl-1*H*-pyrazolyl)methyl][(2-furanyl)methyl]amine (L₁): yield: 0.207 g (94%). ¹H-NMR (500 MHz, CDCl₃): δ (ppm) 2.03 (s, 6H, Pz-CH₃), 2.19 (s, 6H, Pz-CH₃), 3.76 (s, 2H, furan-CH₂), 4.88 (s, 4H, Pz-CH₂), 5.79 (s, 2H, Pz-H), 6.22–6.23 (d, 1H, furan-H), 6.30–6.31 (m, 1H, furan-H), 7.33–7.34 (m, 1H, furan-H). ¹³C-NMR (125 MHz, CDCl₃): δ (ppm) 10.4 (s, CH₃-Pz), 13.4 (s, CH₃-Pz), 45.7 (s, N-CH₂-furan), 64.2 (s, N-CH₂-Pz), 105.8 (s, CH(Pz)), 109.0 (s, CH(furan)), 110.3 (s, CH(furan)), 140.0 (s, C(Pz)), 142.0 (s, CH(furan)), 147.5 (s, C(Pz)), 151.4 (s, C(furan)). ESI-MS $(m/z \ (\%))$: $[L_1 + H^+] = 313.9 \ (20\%), \ [L_1 + Na^+] = 336.1$ (70%). Anal. Calcd. for C₁₇H₂₃N₅O: C, 65.15; H, 7.40; N, 22.35. Found C, 65.09; H, 6.71; N, 21.53. For bis[(3,5-dimethyl-1Hpyrazolyl)methyl][(2-thiophenyl)methyl]amine (L_2): 0.213 g (93%). ¹H-NMR (500 MHz, CDCl₃): δ (ppm) 2.10 (s, 6H, Pz-CH₃), 2.19 (s, 6H, Pz-CH₃), 3.88 (s, 2H, thiophene-CH₂), 4.95 (s, 4H, Pz-CH₂), 5.80 (s, 2H, Pz-H), 6.89–6.91 (m, 2H, thiophene-H), 7.17– 7.19 (m, 1H, thiophene-*H*). ¹³C-NMR (125 MHz, CDCl₃): δ(ppm) 10.7 (s, CH₃-Pz), 13.4 (s, CH₃-Pz), 46.9 (s, N-CH₂-thiophene), 64.6 (s, N-CH₂-Pz), 105.7 (s, CH(Pz)), 124.9 (s, CH(thiophene)), 126.1 (s, CH(thiophene)), 126.5 (s, CH(thiophene)), 140.0 (s, C(Pz)), 141.9 (s, C(thiophene)), 147.7 (s, C(Pz)). ESI-MS (m/z (%)): $[L_2 + H^+] = 329.8$ (30%), $[L_2 + Na^+] = 352.1$ (30%). Anal. Calcd. for C₁₇H₂₃N₅S: C, 61.97; H, 7.04; N, 21.26. Found C, 61.37; H, 6.89; N, 19.60. For bis[(3,5-dimethyl-1H-pyrazolyl)methyl][(2thiophenyl)-ethyl] amine (L₃): 0.225 g (95%). ¹H-NMR (500 MHz, CDCl₃): δ (ppm) 2.15 (s, 6H, Pz-CH₃), 2.20 (s, 6H, Pz-CH₃), 2.71, 2.72 and 2.74 (t, 2H, thiophene-CH₂), 2.94, 2.95 and 2.97 (t, 2H, $N-CH_2$, 4.93 (s, 4H, Pz-CH₂), 5.80 (s, 2H, Pz-H), 6.61 - 6.63 (m, 1H, thiophene-H), 6.85-6.86 (m, 1H, thiophene-H), 7.06-7.07 (m, 1H, thiophene-H). ¹³C-NMR (125 MHz, CDCl₃): δ (ppm) 10.8 (s, CH₃-Pz), 13.4 (s, CH₃-Pz), 28.1 (s, CH₂-CH₂-thiophene), 51.5 (s, CH₂-CH₂-N), 65.7(s, N-CH₂-Pz), 105.87 (s, CH(Pz)), 123.2 (s, CH(thiophene)), 124.7 (s, CH(thiophene)), 126.7 (s, CH(thiophene)), 139.7 (s, C(Pz)), 142.4 (s, C(thiophene)), 147.7 (s, C(Pz)). ESI-MS (m/z (%)): $[L_3 + H^+] = 343.8 (100\%), [L_3 + Na^+] =$ 366.1(30%). Anal. Calcd. for C₁₈H₂₅N₅S: C, 62.94; H, 7.34; N, 20.39. Found C, 63.20; H, 7.10; N, 19.77. For bis[(3,5-dimethyl-1*H*-pyrazolyl)methyl][(2-pyridinyl) methyl]amine (L₄): ¹H-NMR (500 MHz, CDCl₃): δ (ppm) 2.01(s, 6H, Pz-CH₃), 2.18 (s, 6H, Pz-CH₃), 3.87 (s, 2H, Py-CH₂, 4.98 (s, 4H, Pz-CH₂), 5.76 (s, 2H, Pz-H), 7.11-7.16 (m, 2H, Py-H), 7.56-7.59 (m, 1H, Py-H), 8.47-8.48 (d, 1H, Py-H). ¹³C-NMR (125 MHz, CDCl₃): δ (ppm) 10.6 (s, CH₃-Pz), 13.4 (s, CH₃-Pz), 54.6 (s, N-CH₂-Py), 64.9 (s, N-CH₂-Pz), 105.7 (s, CH(Pz)), 122.0 (s, CH(Py)), 123.1 (s, CH(Py)), 136.4 (s, CH(Py)), 139.9 (s, C(Pz)), 147.7 (s, C(Pz)), 148.8 (s, CH(Py)), 158.7 (s, C(Py)). ESI-MS (m/z (%)): [L₄ + H⁺] = 324.8 (100), [L₄ +

Na⁺] = 347.2 (70%). For $C_{18}H_{24}N_6$: C, 66.43; H, 7.74; N, 25.82. Found C, 66.22; H, 7.29; N, 24.85.

Synthesis of compounds 1-4

Complexes 1-4 were synthesized by a common procedure as follows: To a THF solution (2 mL) of FeCl₂·4H₂O (199 mg, 1.0 mmol) was added THF solution (8 mL) of L₁ (313 mg, 1.0 mmol), L₂ (329 mg, 1.0 mmol), L₃ (343 mg, 1.0 mmol) or L₄ (324 mg, 1.0 mmol). The reaction mixture was stirred at r.t. for 6 h, then the solvent removed under reduced pressure. The resulting solid residue was washed with Et₂O (3×20 mL) to afford complexes 1-4 as yellow solid. For 1, Yield: 312 mg (71%). IR (KBr)/cm: v(C = N(Pz)) 1552(s). ESI-MS (m/z (%)): [FeL₁Cl]⁺ = 404.0 (100). Anal. Calcd. for C₁₇H₂₃N₅OFeCl₂: C, 46.39; H, 5.27; N, 15.91. Found: C, 46.11; H, 5.18; N, 15.79. For 2, Yield: 337 mg (74%). IR $(\text{KBr})/\text{cm}: \upsilon(C = N(\text{Pz}))$ 1551(s). ESI-MS $(m/z \ (\%)): [\text{FeL}_2\text{Cl}]^+ =$ 420.0 (100). Anal. Calcd. for C17H23N5SFeCl2: C, 44.76; H, 5.08; N, 15.35. Found: C, 44.12; H, 4.74; N, 14.65. For 3, Yield: 371 mg (79%). IR (KBr)/cm: v(C=N(Pz)) 1553(s). ESI-MS (m/z (%)): $[FeL_3Cl]^+ = 434.0$ (100). Anal. Calcd. for $C_{18}H_{25}N_5SFeCl_2$: C, 45.97; H, 5.36; N, 14.89. Found: C, 45.84; H, 5.37; N, 14.45. For 4, Yield: 383 mg (85%). IR (KBr)/cm: v(C=N(Pz)) 1554(s). ESI-MS $(m/z \ (\%))$: [FeL₄Cl]⁺ = 415.1(100). Anal. Calcd. For C₁₈H₂₄N₆FeCl₂: C, 47.92; H, 5.36; N, 18.63. Found: C, 47.86; H, 5.20; N, 18.15.

X-ray crystallography

Diffraction measurements were conducted at 100(2)–293(2) K on a Bruker AXS APEX CCD diffractometer by using Mo-K α radiation ($\lambda = 0.71073$ Å). The data were corrected for Lorentz and polarization effects with the SMART suite of programs and for absorption effects with SADABS.¹³ Structure solutions and refinements were performed by using the programs SHELXS-97^{14a} and SHELXL-97^{14b} The structures were solved by direct methods to locate the heavy atoms, followed by difference maps for the light non-hydrogen atoms. Anisotropic thermal parameters were refined for the rest of the non-hydrogen atoms. Hydrogen atoms were placed geometrically and refined isotropically.

Catalytic reactions

General method for cross-coupling catalysis runs: After standard cycles of evacuation and back-fill with pure N₂, catalyst (0.05 mmol, 5.0 mol%) was introduced into a 25 mL Schlenk tube equipped with a magnetic stir bar. To the catalyst were added THF (2 mL), alkyl halide (1.0 mmol) and the solution was stirred at r.t.. Aryl Grignard (2.0 mmol) was added dropwise within 30 min and the resulting mixture was stirred for another 10 min. The reaction was quenched with HCl (aq., 2 M, 5 mL). The organic phase was extracted with Et₂O (3×5 mL) and dried over MgSO₄. Mesitylene as internal standard (0.5 mmol, 0.069 mL) was added and then the solvent was carefully removed on a rotary evaporator.

Conclusions

We have demonstrated the catalytic efficacy of Fe(II) aminepyrazolyl complexes towards aryl Grignard coupling with alkyl halides. The coordination mode of the hybrid ligands in these complexes depends on the nature of the tether function on the central amine moiety whereas the metal geometry is in turn governed by the coordination state of the ligand. The use of such flexible multidentate hybrid ligands can stabilise both metals (Fe(II) and Mg(II)) through complexation and solubilisation as well as catalyse Grignard cross-couplings under ambient conditions. They could in principle also be able to give intermetallic (Fe–Mg) species, whose formation could support the aryl transfer across the metals. Current direction in our laboratory is directed at the design of intermetallic complexes supported by suitable tripodal or polydentate ligands and their use as single-site catalysis for cross-couplings.

Acknowledgements

We acknowledge the National University of Singapore and the Ministry of Education (WBS No: R-143-000-361-112) for financial support.

Notes and references

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