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Activation of sp^3 and sp^2 C-H bonds of oxygen containing heterocyclic molecules for alkylation and arylation reactions catalyzed by an iron complex

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Abstract

Activation of both sp^3 and sp^2 C-H bonds is reported using an efficient and iron(III) complex (**1**) of a ligand (N2,N6-bis(2,6-diisopropylphenyl)pyridine-2,6-dicarboxamide: **L**). The iron(III) complex showed catalytic activity of C-C coupling reaction of oxygen containing heterocycles, e.g. tetrahydrofuran (THF), with various alkyl, allyl and aryl Grignard reagents under ambient reaction conditions. Complex **1** demonstrated excellent activity and reactions were completed within 30 min to 1 h. A high turnover frequency (TOF) of 1700 h^{-1} using a low catalyst loading of 0.02 mol% was obtained for the reaction. Interestingly, the catalyst was selective in activation of the C-H bond adjacent to the oxygen in various oxygen containing heterocyclic molecules to yield 2-substitituted products.

Keywords: iron(III) complex; oxygen containing heterocyclics; Grignard reagents; sp^3 and sp^2 C-H bond activation; C-C coupling

1. Introduction

The use of atom efficient and economical methods for the development of complex structures or molecules is always fascinating and challenging tasks for chemists. Various organic synthetic processes strive to employ simple and readily available precursors for the generation of more complex synthetic compounds. C-C coupling reactions by the transformation of functionalities present in the precursor molecule structures are one such field of great scientific interest [1, 2]. Based on the use of different coupling partners, several methods have been established extensively for numerous synthetic applications. These well-defined reactions generally employ compounds with various functionalities present within (or) introduced into the precursor's structure such as alkyl halides [3-7] and olefins [8, 9]. Such nucleophiles have been reported to be easily functionalized with organometallic reagents, for example alkyl and aryl boronic acid [10], tetraalkyltin reagents [11] and Grignard reagents [12]. However, the direct activation of C-H bond and functionalization with Grignard reagent for the C-C coupling reactions has not been exploited [13-15]. The ready availability of a C-H group, which is far more abundant in general organic moieties over other functional groups, has vastly prompted the study of C-H transformation for organic syntheses.

Extensive studies in the last four decades [16-31] has assisted in the better understanding of C-H bond activation. Among these, the use of a transition metal and its complexes as catalysts [32] for C-H bond activation is highly desirable. Transition metals like palladium [33], iridium [34], rhodium [32], platinum [35], nickel [36], cobalt [12], etc. have been reported to play a predominant role to facilitate efficient transformations through C-H activation. However, recent use of 1st row transition metals has caught the attention for performing C-H transformation reactions. Of these, the use of iron complexes as a virtue of their ready availability, low cost,

relatively low toxicity, and unique catalytic abilities has drawn much interest for the activation and transformation of organic/inorganic substrates [37].

Tolman et al. first reported the use of an iron complex for such C-H bond cleavage in the late 1970s. A transient 16-electron iron(0) species, iron(dmpe)$_2$, was accounted for performing the C-H bond cleavage [38]. Photolysis of the associated iron complex, iron(dmpe)$_2$H$_2$, was found to activate C-H bonds of alkenes via generation of the same transient species, iron(dmpe)$_2$ [24]. However, it was the activation of an aromatic C-H bond attained by irradiation of an iron complex, which resulted in the first successful C-H functionalization through catalytic insertion of isocyanide [39].

The use of an iron-based catalyst is even more attractive as iron is cheap and environmentally benign. In 2008, Tatsumi and co-workers reported a half-sandwich iron complex that could carry out reversible C-H bond activation of the 2-position of thiophenes and furans under ambient conditions to produce the iron-heteroaryl complexes [40]. This iron complex was successfully used to synthesize 2-boryl-heteroarenes intermediates upon treatment with catecholborane. However, it was Nakamura et al. in 2008 who developed the first iron based C-H activation for direct arylation. The use of zinc chloride and an aryl Grignard reagent led to the *in situ* generation of an organozinc reagent that was oxidatively coupled with the help of tetramethylenediamine (TMEDA) and 1,10-phenanthroline [34]. Afterwards, the same group successfully functionalized the *ortho* C-H bond of an aromatic ketamine using an arylzinc reagent [41].

The successful activation of C(sp^2)-H bond using various transition metals [12, 33, 42], including iron complexes, encouraged the researcher to investigate the possible use of iron for the largely dormant field of C(sp^3)-H activation and functionalization. However, the activation of

a sp^3 C-H bond is much more complex and, hence, reports are limited [43-45]. This may be a result of the kinetic advantage that sp^2 C-H bonds possess due to the presence of π orbitals, which interact with the metal center making the sp^2 C-H bonds easier to activate. It was Nakamura et al. again, who were the first to report the successful activation of α C(sp^3)-H in an N-heterocyclic molecule for coupling with an organozinc or Grignard reagent [44]. In the same year, Daugulis et al. reported the iron-catalyzed deprotonative alkylation of arene C−H bonds by alkyl iodides and bromides [46].

[Figure 1 Here]

Here we report the catalytic cross coupling of Grignard reagents with oxygen containing heterocyclic molecules, e.g. tetrahydrofuran (THF), by the activation of the C-H bond (Figure 1). Catalyst **1** was able to activate the sp^3 C-H bond α to the heteroatom, leading to a 2-substituted cross-coupled product. Similar activation of α C-H bonds in unsaturated heterocyclic molecules (sp^2 C-H bond), e.g. thiophenes and furans, is known in the literature [40]. Direct sp^3 C–H arylation and alkylation at the α-position of cyclic aliphatic ethers using iron oxide as catalyst has also been recently reported by Vishwakarma and co-workers [47, 48]. But to the best of our knowledge, this is the first example of an iron(III) pincer complex (**1)** of a bis(amido)pyridine ligand which was used for catalytic C-H activation and subsequent C-C cross coupling reactions using Grignard reagents as coupling partners. Furthermore, the uniqueness of this work also lies in its ability to activate both sp^3 and sp^2 C-H bonds in various oxygen containing heterocyclic molecules. Besides these, the ability to perform the reactions under ambient reaction conditions without the need of any special equipment or reaction conditions indicates the catalytic

effectiveness of **1**. The catalyst (**1**) showed excellent activity with reactions completed in 30 minutes to 1 h. A turnover frequency (TOF) of 1700 h^{-1} was obtained with a catalyst loading of only 0.02 mol%.

2. Experimental

2.1 Materials and Methods

All the chemicals and solvents were obtained either from Aldrich Chemical Co., USA or Fisher Scientific Company, USA and used as obtained without further purifications unless otherwise stated. Tetrahydrofuran (THF) was purified according to the literature procedure [49]. Electrospray ionization mass spectra (ESI-MS) were obtained using an Agilent 100 series MSD VL spectrometer. Gas Chromatography Mass spectra (GC-MS) were obtained using an Agilent technologies 6890N network GC system and equipped with Agilent Technologies 5975 inert XL mass selective detector. Ultraviolet visible spectra (UV-Vis) were recorded using a Varian Cary 5000 UV-Vis-NIR spectrophotometer. ^{1}H-NMR and ^{13}C-NMR spectra were obtained using a a JOEL ECS400 400 MHz instrument equipped with a 5 mm triple resonance inverse probe. The spectra were collected at 25 °C, and chemical shifts were reported in ppm relative to TMS as external standard. FTIR spectra were obtained using a Thermo Scientific Nicolet 6700 FT-IR spectrometer.

2.2. Synthesis of 1

The pincer ligand was synthesized according to the literature procedure [50]. Ligand (**L**) was deprotonated with n-butyllithium in THF and reacted with anhydrous ferric chloride ($FeCl_3$)

to obtain **1**. Detailed synthetic methods of **L** and **1** are described in our previous reported work [51].

2.3. Cross coupling of tetrahydrofuran with Grignard reagents

Cross coupling reactions of Grignard reagents with tetrahydrofuran were performed according to the following general method. Stock solution of the catalyst in dry THF at the concentration of 1 mg/1 mL was freshly prepared. An aliquot of Catalyst **1** (0.5 mg, 0.87 μmol) in THF was added using a gas-tight syringe to a 5 mL round bottom flask purged with argon. To this solution, 25% phenylmagnesium chloride in THF (0.5 mL, 0.92 mmol) followed by dibromoethane (90 μL, 1.04 μmol) were added and allowed to stir at room temperature. Samples for analysis were collected at the appointed time intervals over a period of 5 min to 60 min. Excess Grignard reagent was destroyed using methanol and the reaction products were quantitated by GC using an internal standard 2-methyltetrahydrofuran. To obtain the calibration curve 7 points were used, with concentrations of internal standard ranging 0-200% of the product yields. For preparative synthesis, work up was done as follows. After the completion of the reaction, 15 mL of saturated ammonium chloride was added to the reaction mixture. The aqueous solution was extracted with ethyl acetate (3x 20 mL) and the organic solution was dried ($MgSO_4$), filtered, and the solvents removed under reduced pressure. Compounds were visualized under UV lamp or by developing in iodine. Medium pressure liquid chromatography (MPLC) separations were carried out using commercially available silica gel columns and technical grade solvents.

2.4. Cross coupling of oxygen containing heterocyclics with Grignard reagents

Cross coupling reactions of Grignard reagents with other heterocyclics such as furan and dioxane were performed according to the following general method.

An aliquot of Catalyst **1** (0.5 mg, 0.87 μmol) in diethyl ether was added using a gas-tight syringe to a 5 mL round bottom flask purged with argon. To this solution, phenylmagnesium chloride in ether (0.92 mmol) followed by dibromoethane (90 μL, 1.04 μmol) were added and allowed to stir at room temperature. Samples for analysis were collected at the appointed time intervals over a period of 60 min. Excess Grignard reagent was destroyed using methanol and the reaction products were quantitated by GC-MS using an internal standard 2-methyltetrahydrofuran. Product yields were reported in turnover number (TON: moles of product formed per mole of catalyst used) and turnover frequency (TOF: moles of product formed per mole of catalyst in unit time). For large scale synthesis, the compound was worked up and isolated as mentioned above.

3. Results and discussions

Our preliminary studies indicated that (Table 1) the efficient cross coupling reaction required small amount of dibromoethane as additive. A control reaction in the absence of **1**, using THF, phenylmagnesium chloride and dibromoethane yielded very trace amount of reaction product. Addition of very small amount of **1** (0.1 mg; 0.02 mol%) resulted in 32% of the 2-substituted product with a turnover number (TON) of 1700. A ten-fold increase in catalyst used resulted in significant yield of (75%) phenyltetrahydrofuran. However, the high amount of catalyst resulted in the net decrease in the TON. As the use of 0.5 mg of **1** (0.1 mol%) yielded significantly high yield and TON of 64% and 680, respectively; we thus chose to continue with 0.5 mg of catalyst for further optimization reactions.

[Table 1 Here]

Based on the preliminary studies (Table 1), which indicated the need of dibromoethane as an additive, further analysis of the influence of the additives was studied. Different additives similar to dibromoethane were evaluated in C-H activation and coupling reactions, indicating the superiority of dibromoethane over other similar molecules such as dichloroethane. Effect of change in the amount of dibromoethane on the reaction yields was further studied by carrying out reaction using varying amounts of dibromoethane and 0.5 mg of catalyst **1**. Figure 2 shows the yield obtained at 20 min and 1 h of reaction time *vs* different dibromoethane to **1** ratios. As seen in Figure 3, 0.6 to 1.2 equivalents of dibromoethane were sufficient for obtaining effective yields.

[Figure 2 Here]

We studied the reaction kinetics at various catalyst concentrations (Figure 3) based on product formation with respect to time. All the reactions were carried out at room temperature using 90 μL of dibromoethane and 0.5 mL of 25% phenylmagnesium chloride in THF. Samples were collected and analyzed at different time intervals of 5, 20, 40 and 60 minutes.

[Figure 3 Here]

Following this analysis, we studied the effect of temperature on the yield at different temperatures ranging from -15 ^{o}C to 50 ^{o}C. Just 14% of the product was obtained in 20 min at a

reaction temperature of -15 ^{o}C. As revealed in Figure 4, with increasing temperature an increase in the yield of the product was observed. At room temperature, 35% yield with TON of 370 was obtained. Further increase in temperature to 50 ^{o}C yielded 48% of product with TON of 508.

[Figure 4 Here]

The activation of the C-H bond in THF for cross coupling with various other Grignard reagent was also checked using different alkyl Grignard reagents. This C-H activation led to the formation of new sp^3-sp^3 C-C bond. Use of ethylmagnesium chloride as Grignard reagent gave 42% yield with a TOF of 445 h^{-1} (Entry 1, Table 2). While using butylmagnesium choride reagent (Entry 2 Table 2), the yield of the product obtained was about 35%. Further increase in the alkyl chain length to hexylmagnesium chloride (Figure S4, Supporting information) and octylmagnesium chloride led to a decrease in the yields to 28 and 26% and TOF of 297 h^{-1} and 276 h^{-1}, respectively. The use of nonlinear Grignards like isopropylmagnesium chloride yields 29% of the product. In case of cyclopentylmagnesium chloride reagent too similar amount of product yield (30%) was observed. Additionally, the use of allyl Grignard reagent also showed to be effective in cross coupling with the activated C-H, though the yield was significantly lower.

[Table 2 Here]

As it was observed from the initial optimization reactions that the use of phenylmagnesium chloride yielded comparatively more of the desired product, reactions were performed for cross coupling using various aryl Grignard reagents. Use of aryl Grignard reagents

in these reactions showed high efficiency for the formation of a new sp^3(C)-sp^2(C) bond leading to its corresponding 2-substituted phenyl tetrahydrofuran (Figure S9, Supporting information). As seen in the Table 3 (entry 2), use of aryl Grignard reagent phenylmagnesium chloride yielded 66% of 2-phenyl tethydrofuran with a TOF of 700 h^{-1}. The use of its bromide analog increased the yield and TOF of the product to 77% and 816 h^{-1}, respectively (Table 3, entry 1). The iodide form of phenyl Grignard reagent similarly produced the desired product with high yield of 78% and TOF of 827 h^{-1} (Table 3, entry 3). The use of toluenemagnesium iodide (Figure S10, Supporting information) showed further increment in the yield with 82% yield (Table 2, entry 9). Reactions were also done with 2- and 4- methoxy substituted phenylmagnesium bromide. The 2-methoxy substituted phenylmagnesium bromide (Table 3, entry 5) showed slightly higher activity than the 4-methoxy (Table 3, entry 4) substituted one with 79% and 74% yields, respectively. The use of biphenylmagnesium bromide with a phenyl group at the 2 position showed decreased activity as compared to the unsubstituted phenylmagnesium bromide (Figure S12, Supporting information). Steric constraints due to its large size/bulkiness may be one of reasons attributing to the lower activity. The use of bromide and iodides Grignard reagents over the chloride one seemed advantageous, but not to a significant extent.

[Table 3 Here]

The iron complex **1** was also examined for its ability to activate sp^3 C-H bonds and sp^2 C-H in different oxygen containing heterocyclics such as 1,4-dioxane and furan (Table 4). Reaction of six membered 1,4-dioxane resulted in 54% of the 2-substituted product (Table 4, entry 1). However, no disubstituted product was seen (Figure S16, Supporting information). Additionally,

the catalyst **1** was able to activate sp^2 C-H bond in furan (Table 4, entry 2-5). The activation of C-H in furan and further cross coupling with phenylmagnesium chloride resulted in 42% of 2-phenylfuran (Table 4, entry 2) (Figure S13, Supporting information).

[Table 4 Here]

The mechanism by which the iron catalyst **1** catalyzes the C-H activation and further cross coupling occurs is not completely known to us. α C-H bond in THF is a relatively weak bond (~ 80 Kcal/mol) and this bond can be activated easily. It can also be assumed that there is an oxygen directed interaction between the THF molecule and the iron center of the complex. This results in the activation of the α C-H bond in THF. Such heteroatom directed activation of α C-H bonds resulting in 2-substituted products is not new and has been previously reported in the literature. In our study, this form of substitution was confirmed by comparing the product obtained by bubbling methylmagnesium bromide in THF using catalyst **1**. The reaction product with *m/z* 86 (Figure S17, Supporting Information) was found to have the same *m/z* of 86 and retention time of 1.576 min as that of pure 2-methyltetrahydrofuran sample (Figure S18, Supporting Information). Formation of 2-susbtituted products was further proved by isolating the pure products and performing ^{1}H and ^{13}C NMR spectroscopy (Figures S22-S25, supporting information).

Furthermore, the role of a transient intermediate formed upon the addition of the Grignard reagent to the iron complex cannot be refuted for the catalytic conversion. Similar transient intermediates have been previously detected and postulated for coupling reactions involving Grignard reagents [50, 52, 53]. The presence of this non-transient intermediate was

evident in a rapid solution color change (λ_{max} ~ 460-500 nm) upon addition of various Grignard reagents to a solution of **1** in THF (Figure S19a, Supporting Information). The formation of such an intermediate was further confirmed by ESI-MS, for example, the butyl intermediate formed through the interaction of **1** with butylmagnesium chloride was also detected using ESI-MS at *m/z* 597.4 (Figure S19b, Supporting Information) [51].

Another intriguing fact is the exact role of dibromoethane in these reactions, which is not known. Previous report shows that similar molecules such as dichloroethane and dichlorobutane have been used as additives responsible for re-oxidizing the metal center to its original active state. This mechanism of re-oxidizing the metal center using such oxidants is not new and is in accordance with some of the previous C-H activation work reported [36]. We think dibromoethane plays a similar role in our set of reactions for efficient catalysis. The interaction of dibromoethane with the **1** was further confirmed by the presence of bromobenzene (as shown in Figure S20, Supporting Information) as intermediates/side product, which was seen in the interaction of **1**-Br (from **1** and dibromoethane**)** and phenylmagnesium chloride.

Further studies using UV-Vis spectrum showed that the phenyl intermediate which shows the persistent peak at 466 nm, showed marked decrease upon the addition of dibromoethane. Thus, the catalytic cycle is promoted which is observed by the decrease in the peak absorbance (see Supporting information, Figure S21) with respect to time. Additional immediate inspection of the reaction mixture using GC-MS reveals the formation of the desired product phenyltetrahydrofuran. The possibility of a free radical mechanism in the reaction was also checked using excess amount of free radical trap TEMPO in the control reaction. The production of significantly low products negates the possibility of a radical pathway/mechanism. A possible reaction mechanism is presented in the supporting information (see Supporting information,

Scheme S1). However, further mechanistic studies need to be done to confirm the exact mechanism of the reaction system.

4. Conclusions

The iron(III) pincer complex **1** enabled the facile activation of sp^3 C-H bonds in tetrahydrofuran, for cross coupling with various aryl and alkyl Grignard reagents. The reactions proceeded efficiently at room temperature in reaction time of 30 min to 1 h. The complex showed much improvement in activity over that of previously reported similar type of C-H activation and C-C bond formation using Grignard reagents as coupling partners. This method of activation of sp^3 C-H bond and further cross coupling can serve as a route for synthesis of high value added product, under mild conditions. The change in the reaction parameters lead to change in the percent yield of the cross-coupled product, leading to the optimization of the reaction conditions. The catalyst **1** showed high efficiency with TON of 1700 with catalyst loading of just 0.02 mol%. **1** was also found to be efficient in activating sp^2 C-H bond in oxygen containing heterocyclic molecule. Further activation of C-H bond using **1** in various other heterocyclic molecules, particularly in N-heterocyclic molecules is currently under investigation.

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Supporting information

Additional details on the gas chromatograms for reactions involving THF and Grignard reagents using iron(III) complex **1** and the mass spectroscopy of the desired product formed are included in the supplementary information.

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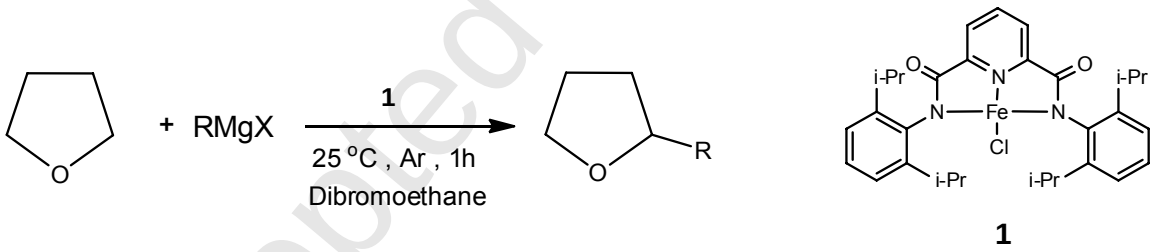


Figure 1: Cross coupling of tetrahydrofuran with Grignard reagents using iron(III) complex **1**.

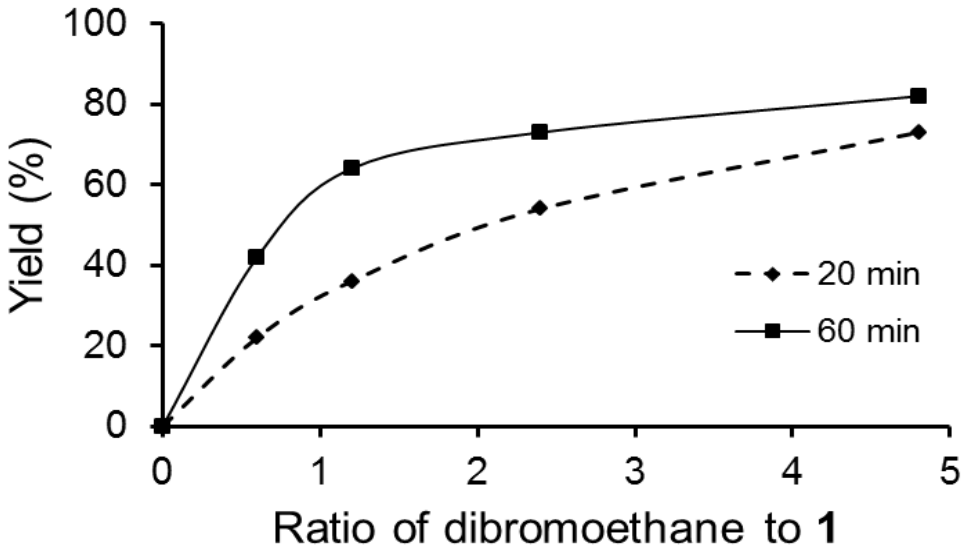


Figure 2: Effect of ratio of dibromoethane to catalyst **1** on the coupling reaction. **1** (0.5 mg, 0.87 µmol), 25% phenylmagnesium chloride in THF (0.5 mL, 0.92 mmol), at room temperature and reaction time 20 min and 60 min.

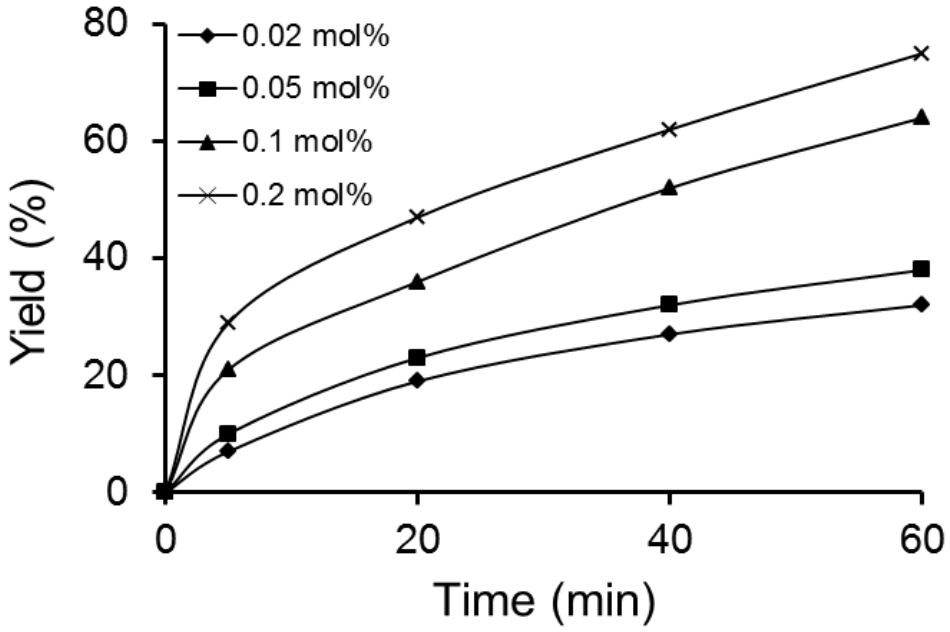


Figure 3: Effect of amount of catalyst **1** on the coupling reaction, with respect to time. **1** (0.1 mg-1 mg), dibromoethane (90 µL, 1.04 µmol), 25% phenylmagnesium chloride in THF (0.5 mL, 0.92 mmol), at room temperature and reaction time of 5 min to 1 h.

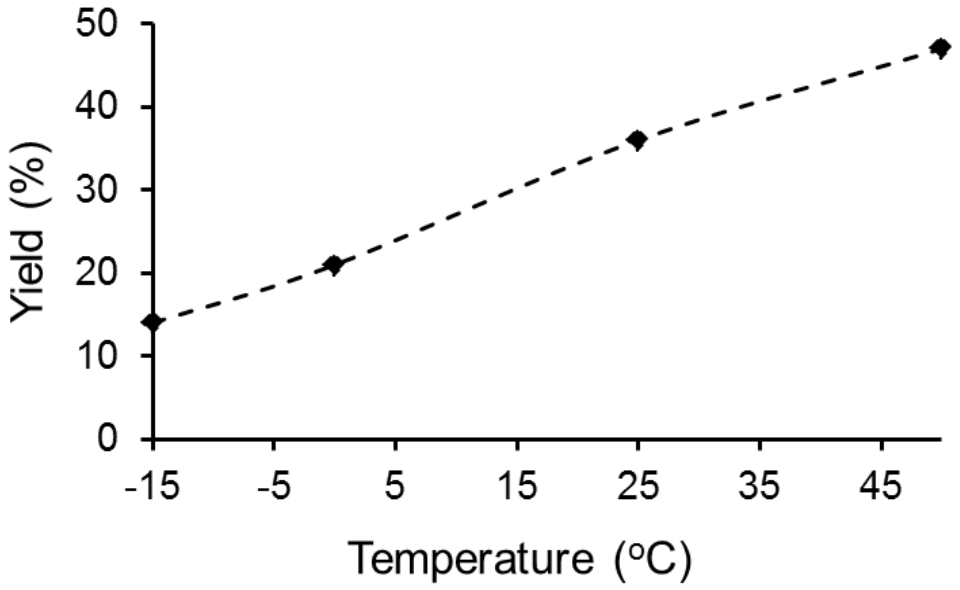


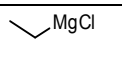
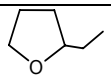
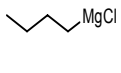
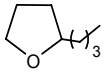
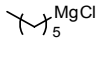
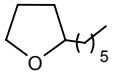
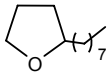
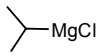
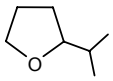
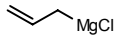
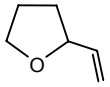
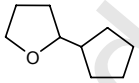
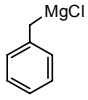
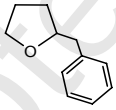
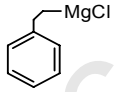
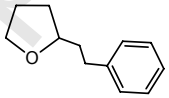
Figure 4: Effect of temperature (-15 °C to 50 °C) on the coupling reaction. **1** (0.5 mg, 0.87 µmol), 25% phenylmagnesium chloride in THF (0.5 mL, 0.92 mmol), dibromoethane (90 µL, 1.04 µmol), reaction time 20 min.

Table 1: TON of different substrate to catalyst ratio reactions.

Entry	Catalyst 1 (mg)	Dibromoethane (µL)	Yield (%)	TON
1	0	90	Trace	-
2	0.1	90	32	1700
3	0.2	90	38	801
4	0.5	90	64	680
5	1	90	75	400
6	0.5	0	16	200

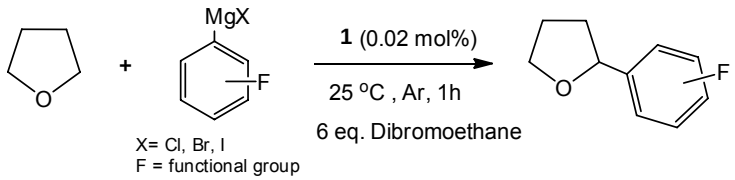
25% Phenylmagnesium chloride in THF (0.5 mL, 0.92 mmol), dibromoethane (90 µL, 1.04 µmol) at room temperature. Reaction time 1 h. Yield (%) is the percentage of phenylmagnesium chloride coupled with THF. Reaction products were quantitated by GC using 2-methyltetrahydrofuran as internal standard.

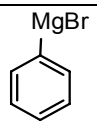
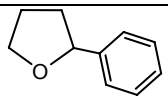
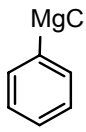
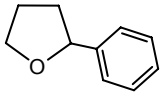
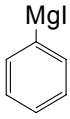
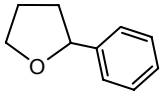
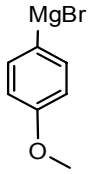
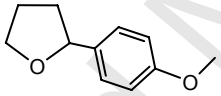
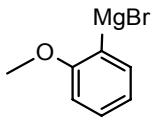
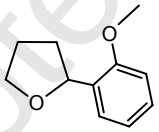
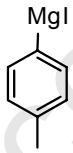
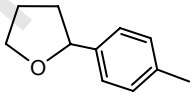
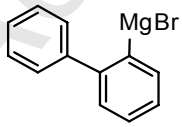
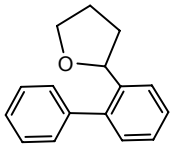
Table 2: Synthesis of substituted tetrahydrofurans using various Grignard reagents.

	Grignard reagent	Product	Time (h)	Yield (%)	TOF (h^{-1})
1			1	42	445
2			1	35	370
3			1	28	297
4			1	26	276
5			1	29	307
6			1	14	148
7			1	30	318
8			1	51	540
9			1	39	413

Grignard reagent in THF (0.92 mmol), Dibromoethane (90 µL, 1.04 µmol) at room temperature. **1** (0.5 mg, 0.87 µmol), reaction time 1 h. Yield (%) is the percentage of Grignard reagent coupled with THF. Reaction products were quantitated by GC using 2-methyltetrahydrofuran as internal standard.

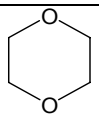
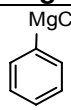
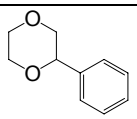
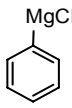
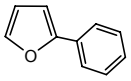
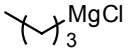
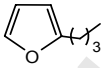
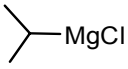
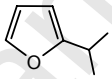
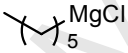
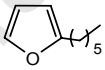
Table 3: Cross coupling using various substituted phenyl Grignard reagents.



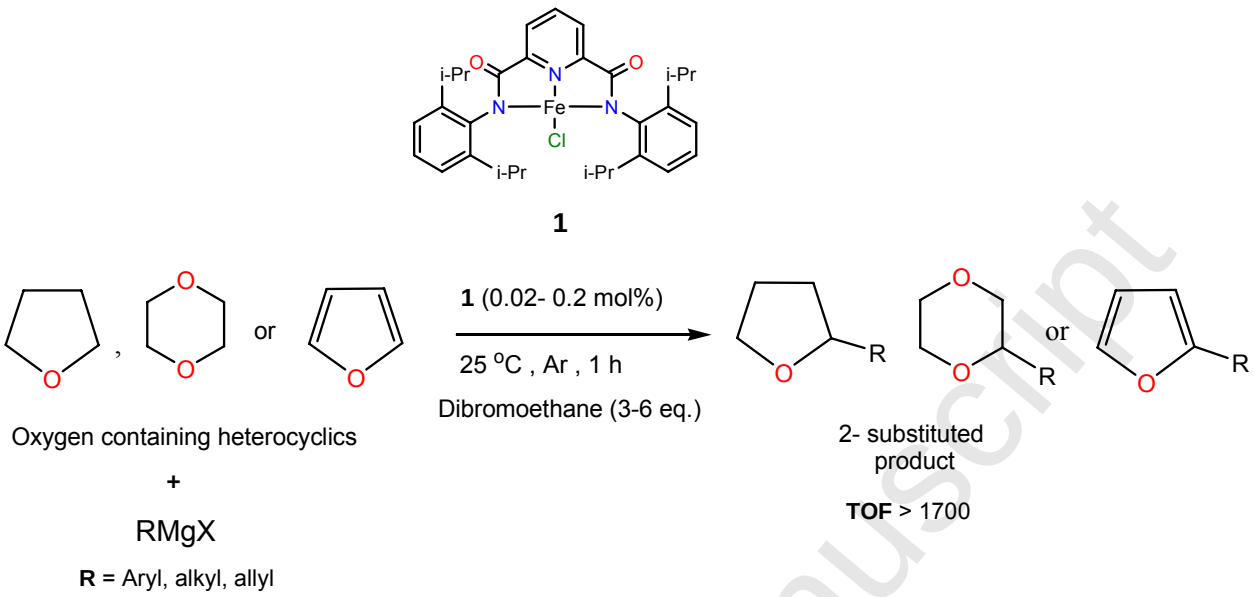
	Grignard reagent	Product	Time (h)	Yield (%)	TON
1			1	77	816
2			1	66	700
3			1	78	827
4			1	74	784
5			1	79	837
6			1	82	869
7			1	61	646

Grignard reagent in THF (0.92 mmol), dibromoethane (90 µL, 1.04 µmol) at room temperature. Reaction time 1 h. Yield (%) is the percentage of Grignard reagent coupled with THF. Reaction products were quantitated by GC using 2-methyltetrahydrofuran as internal standard.

Table 4: C-H activation of different oxygen containing heterocyclic molecules for cross coupling with Grignard reagents.

Entry	Heterocyclic substrate	Grignard reagent	Product	% Yield
1				54
2				42
3				33
4				32
5				27

Grignard reagent in diethyl ether (0.92 mmol), dibromoethane (90 µL, 1.04 µmol) at 25 ^{o}C. Reaction time 1 h. Yield (%) is the percentage of Grignard reagent coupled with the oxygen containing heterocyclic molecule. Reaction products were quantitated by GC using 2-methyltetrahydrofuran as internal standard.



Graphical abstract

- Highlights
- An efficient iron(III) complex of an bis(amido)pyridine ligand for activation of sp^3 and sp^2 C-H bonds.
- C-C coupling of oxygen containing heterocyclics with various alkyl, allyl and aryl Grignard reagents.
- Activation of selective α C-H bond at room temperature and within a short period of time.
- Low catalyst loading (0.02- 0.2 mol%) and high turnover frequency (>1700 h^{-1}).