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PAPER

New method for C–H arylation/alkylation at α-position of cyclic aliphatic ethers by iron-oxide mediated reaction†

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We report a new and efficient iron oxide catalyzed cross-coupling reaction between organometallic species such as alkyl/arylmagnesium halides or organolithium species and α-hydrogen bearing cyclic unbranched and branched aliphatic ethers *via* activation of C(sp^3)–H. In the presence of 1 mol% of iron oxide, five and six membered unbranched cyclic ethers such as tetrahydrofuran and tetrahydropyran gave good to excellent yields of cross-coupled products. Whereas, in case of branched ether such as 2-methyltetrahydrofuran, it was observed that the arylation occurred at both the sides and gave moderate yields of a mixture of regioisomers. Among the organometallic species used, alkyl organometallic reagents gave less yields as compared to aryl organometallics.

Introduction

Metal catalyzed cross-coupling reactions for C–C bond formation *via* the activation of C(sp^2)–H or C(sp^3)–H is a major topic of current research,[1,2] attracting many research groups all over the world. Traditionally, a cross-coupling reaction involves two starting materials; organometallic species (RMgX or RLi) and organic halide (C–Y). However, replacing organic halides (C–Y) with a C–H species is a far more efficient coupling strategy, which deserves greater attention.[3] In the last two decades, various transition metal catalyzed cross-coupling reactions *via* the activation of C(sp^2)–H have been developed,[4] but the examples of such cross-coupling through the activation of C(sp^3)–H are limited.[5]

In our preliminary work,[6] we observed that iron oxide catalyzed cross-coupling reactions between organometallic halides and α-hydrogen bearing cyclic ethers such as tetrahydrofuran led to C–C bond formation *via* direct activation of the C(sp^3)–H centre. We have now built up on this interesting finding and expanded it for full utilization. We have explored our method for the cross-coupling of aliphatic and aromatic organometallic species with various five and six membered branched and unbranched cyclic ethers *via* α-C(sp^3)-H activation. Attempts towards the cross-coupling reaction of organometallic species with other cyclic ethers such as oxetane and dioxane as well as acyclic ethers were also tried, without success. We explored this new C–C bond formation for the synthesis of 2-substituted furans and pyrans using iron oxide catalysis. Since many biologically active natural products are comprised of tetrahydrofuran or tetrahydropyran scaffolds with substituents α to the oxygen atom,[7,8] this reaction offers tremendous potential for introducing groups into the α-position of cyclic ethers strategically important for synthesis. This work was inspired by an unprecedented observation in our lab on the formation of 2-phenyltetrahydrofuran instead of 2-phenylbutane during a reaction of phenylmagnesium bromide with 2-bromobutane in the presence of TMEDA and catalytic amount of $FeCl_3$. Recently, Yoshikai *et al.*[5b] developed an efficient iron catalyzed C–C bond formation at the α-position of aliphatic amines *via* C(sp^3)–H bond activation as an unexpected finding during the reaction of Ph_2Zn and 4-iodotoluene in THF in the presence of an iron-bispyridine catalyst, yielding 2-phenyltetrahydrofuran instead of the expected biaryl product. These findings provoked interest in us to further explore this reaction. Careful examination of the catalyst used suggested that the old bottle of $FeCl_3$ used by us contained substantial quantity of iron hydroxide. In last two decades, iron based catalysts[5b,5c,9] have drawn the attention as cheap, nontoxic and environmental friendly materials for the generation of radicals[5b,5c,10] as well as activation of electrophilic substrates.[11] Keeping in mind the radical chemistry literature of iron and recent finding regarding the role of aluminium-vanadium oxides in C–H activation *via* hydrogen abstraction,[12,13,14] we envisioned that iron oxides could be utilized for cross-coupling reactions of organometallic species with an unactivated ethers *via* activation of the C(sp^3)–H bond.

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† Electronic supplementary information (ESI) available: $^1H/^{13}C$ NMRs, DEPT, GCMS, *etc* of all compounds is attached (55 pages). Tables containing chemical shift value of CH-Ar and CH-Alkyl are also enclosed in the ESI. See DOI: 10.1039/c1ob06660a

Result and discussion

We selected various iron salts *viz.*, $Fe(OH)_3$, $FeCl_3$ and Fe_2O_3 to test the idea and started this study by the reaction of phenylmagnesium bromide with unactivated cyclic ether such as THF (results summarized in Table 1). During our study, THF was used also as a solvent. When we examined the reaction of phenylmagnesium bromide **1a** with THF in the presence of 10 mol% of $Fe(OH)_3$ at room temperature, the desired 2-phenyltetrahydrofuran **2a** was obtained in 40% yield together with biphenyl **3**, phenol **4** and bis-phenol **5** (Table 1, entry a) as byproducts. The use of fresh anhydrous $FeCl_3$ decreased the chemical yield of **2a** to less than 5% along with the formation of biphenyl **3** in less than 8% yields (Table 1, entry b). Interestingly, the use of 10 mol% of Fe_2O_3 at room temperature increased the chemical yield of **2a** from 40% to 77% (Table 1, entry c). Furthermore, we found that lowering the amount of Fe_2O_3 catalyst (from 10 mol% to 1 mol%) and temperature (from rt to 0 °C) greatly affected the chemical yield of **2a** (Table 1, entry d–h). For example, 1 mol% of Fe_2O_3 at 0 °C increased the yield of **2a** from 77% to 95% and suppressed the formation of undesired byproduct (Table 1, entry h). However, further lowering of temperature *i.e.*, −10 °C and −70 °C did not show much improvement in yield of **2a** and a longer reaction time was required for completion (Table 1, entry e and f).

When this reaction was attempted in the absence of Fe_2O_3, no product formation was observed even after a prolonged reaction. As can be seen from Table 1, the cheap and non-hygroscopic iron oxide (Fe_2O_3) is the most appropriate catalyst from the practical point of view. Furthermore, our investigation suggested that the cross-coupling reaction of organometallic species with α-hydrogen bearing ethers *via* activation of $C(sp^3)$–H did not require expensive or toxic ligands (Scheme 1).

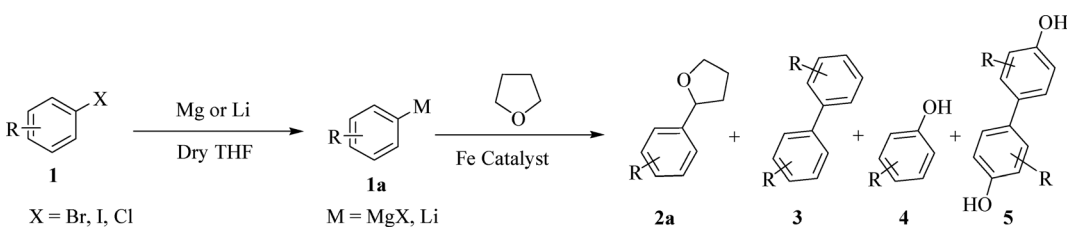
The reactivity of various organometallic species such as Grignard reagents and organolithiate species towards five membered cyclic ethers such as THF and 2-methyltetrahydofuran (2-MTHF) was investigated (Table 2 and Table 3). Aryl and heteroaryl Grignard reagents bearing different substituent on reaction with THF provided the desired products **2a–m** in moderate to excellent yields with 1 mol% of Fe_2O_3. Substrates possessing electron-donating (Table 2, entries c–h) and electron-withdrawing groups (Table 2, entries i–k) at the aryl magnesium halide moiety smoothly underwent cross-coupling reaction to afford corresponding 2-phenyltetrahydrofuran in high yields. Moreover, hindered 1-napthylmagnesim bromide underwent cross-coupling, affording 2-napthyltetrahydrofuran in good yield (Table 2, entry l). Heteroarylmagnesium bromide such as 2-(5-methylthiophenyl)magnesium bromide also coupled with THF and afforded 2-(5-thiophenyl)tetrahydrofuran in moderate yield (Table 2, entry m). Aryl lithium species (Table 2, entry n, o–q) underwent cross-coupling reactions with cyclic ether THF and gave desired products **2n–q** in good to excellent yields. The present approach is also applicable to both primary (Table 2, entries r–t) as well as secondary aliphatic (Table 2, entry u) organometallic species, although the yields of aliphatic organometallic species are comparatively less than the aromatic organometallic species. The reaction of allylmagnesium bromide was sluggish (Table 2, entry v) and the desired product **2v** was obtained in very low yield along with a mixture of unidentified products.

Furthermore, in case of branched five membered cyclic ethers such as 2-methyltetrahydrofuran, the coupling was moderate with the formation of a mixture of two unseparable regioisomers **6** and **7**, which were generated by the attack of organometallic species at the unsubstituted and substituted side of 2-MTHF respectively. Aryl organometallic species bearing a phenyl ring, napthyl ring and *p*-chlorophenyl (Table 3, entries a, c, d, e, g

Table 1 Screening of different iron based catalysts

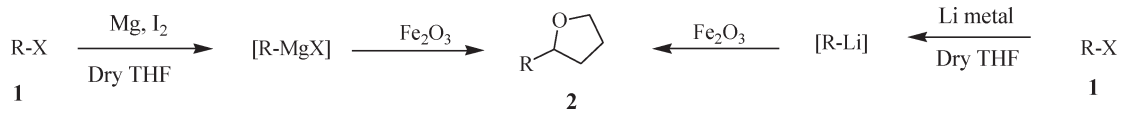
					Yield (%)[a]			
Entry	Catalyst	Catalyst quantity	Temperature	Time (h)	**2a**	**3**	**4**	**5**
a	$Fe(OH)_3$	10 mol (%)	rt	8	40	10	20	5
b	$FeCl_3$	10 mol (%)	rt	8	<5	8	—	—
c	Fe_2O_3	10 mol (%)	rt	8	77	4	7	1
d	Fe_2O_3	10 mol (%)	0 °C	8	85	3	1	—
e	Fe_2O_3	10 mol (%)	−10 °C	12	92	2	1	—
f	Fe_2O_3	10 mol (%)	−70 °C	12	90	2	1	—
g	Fe_2O_3[a]	10 mol (%)	−10 °C	8	85	5	8	—
h	**Fe_2O_3**	**1 mol%**	**0 °C**	8	**95**	—	0.5	—

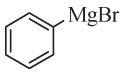
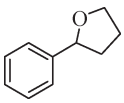
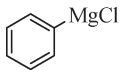
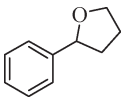
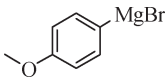
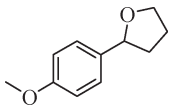
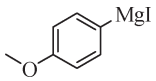
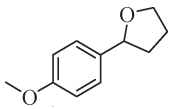
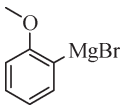
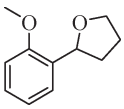
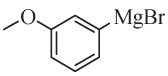
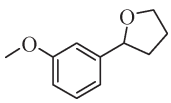
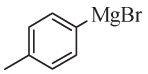
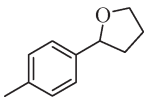
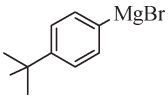
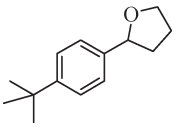
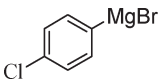
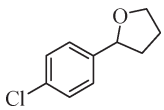
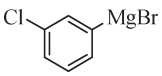
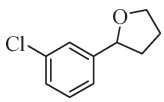
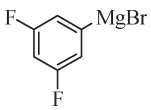
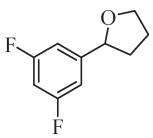
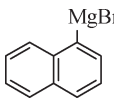
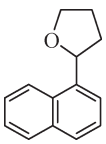
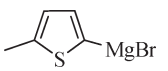
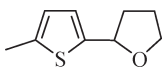
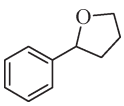
[a] HPLC yield.



Scheme 1 Iron oxide catalyzed cross-coupling reaction of organometallic species with THF *via* activation of α-$C(sp^3)$-H.

Table 2 Iron oxide catalyzed cross-coupling reaction of organometalhc species with THF *via* activation of α-C(sp^3)-H



Entry	RMgX/RLi	Product (**2**)	Time (h)	Yield (%)[a]
a			5	95
b			5	92
c			6	89
d			6	93
e			5	92
f			6	91
g			6	94
h			6	91
i			6	96
j			5	96
k			5	93
l			6	91
m			10	70
n			8	89

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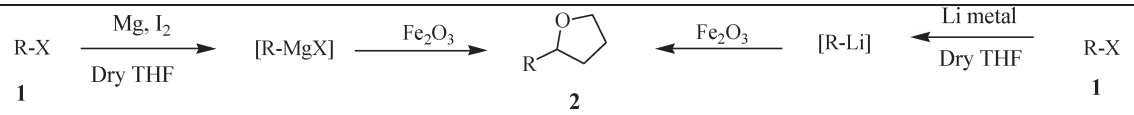

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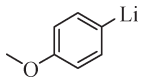
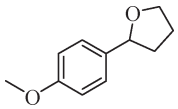
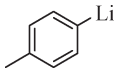
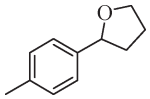
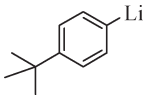
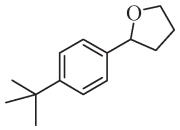
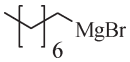
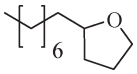
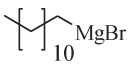
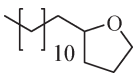
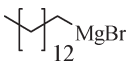
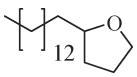
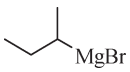
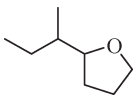
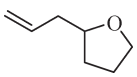
o			9	87
p			8	85
q			10	85
r			8	49
s			10	46
t			10	41
u			9	47
v			8	10

All reactions carried out in THF in the presence of Fe_2O_3 (1 mol%),[a] Isolated yield.

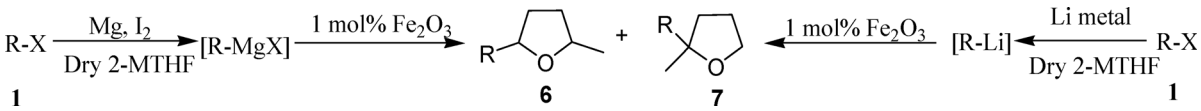
and h) on coupling with 2-MTHF gave a mixture of cross-coupled products, **6** (as minor isomer) and **7** (as major isomer), whereas organometallic species bearing *p*-methoxyphenyl ring (Table 3, entry b and f) gave the mixture of **6** and **7** isomers in almost equal quantities. GC and ^{1}H NMR spectroscopy were used to determine the composition of regioisomeric product mixtures. The formation of major isomer **7** on reaction with 2-MTHF suggested that the cross-coupling reaction might follow a radical mechanism, whereas in case of the *p*-methoxyphenyl ring both the regioisomers formed in equal quantities which might be because of steric hindrance due to the methoxy group. Overall, in case of 2-MTHF, yields were comparatively less as compared to THF.

In order to understand the diversity of present methods, we also explored the cross-coupling reaction of organometallic species with six membered cyclic ethers *viz*., tetrahydropyran (THP) under optimized conditions. Various Grignard reagents underwent cross-coupling reactions with THP and afforded the desired products **8a–d** in good to excellent yields with 1 mol% Fe_2O_3 and the results are summarised in Table 4. Phenylmagnesium bromide (Table 4, entry a) reacted with THP and gave the desired cross-coupled product in 94% yield. Both electron-donating (Table 4, entry b) and as well as electron-withdrawing group (Table 4, entry d) containing arylmagnesium halides also gave desired product in excellent yields. Hindered 1-napthylmagnesium bromide also underwent cross-coupling and gave the desired 2-napthyltetrahydropyran in good yield (Table 4, entry c). Similarly, Fe_2O_3 also catalysed the cross-coupling reaction of various aryl lithium species (Table 4, entries e–h) with THP and gave the desired coupled product **8e–h** in good to excellent yields as summarised in Table 4.

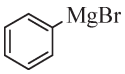
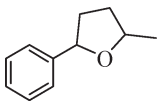
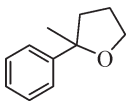
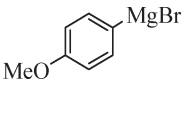
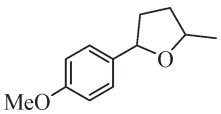
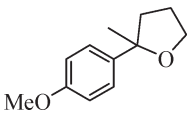
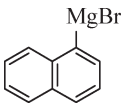
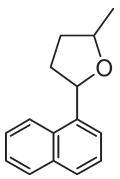
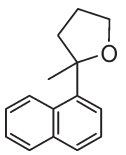
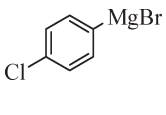
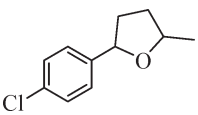
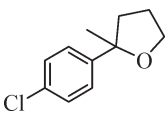
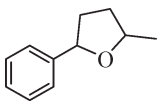
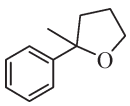
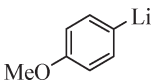
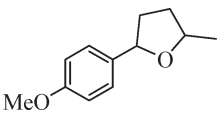
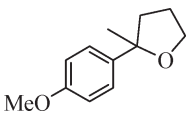
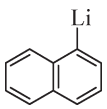
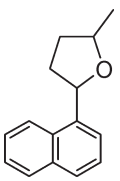
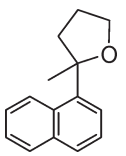
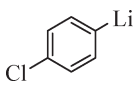
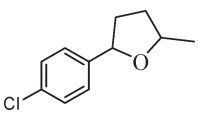
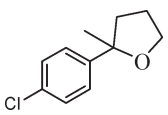
Further, cross-coupling reactions of organometallic species with other α-hydrogen bearing ethers such as dioxane and four membered cyclic ethers *viz*., oxetane were also tried under optimized conditions. The reaction of Grignard reagent with oxetane was sluggish and gave a mixture of phenol and biphenyl, along with some unidentified products. The cross-coupling reaction of Grignard reagent with dioxane in the presence of Fe_2O_3 did not give a cross-coupled product even at heating.

Studies towards the coupling of various organometallic species with various α-hydrogen bearing acyclic ethers was also investigated (Scheme 2). Both primary ethers *viz*., diethyl ether as well as secondary ethers *viz*., diisoprpoyl ether were tried and neither of the acyclic ethers underwent the cross-coupling reaction, but on stirring for longer times, the formation of 1-arylethanol **11** was observed. The formation of 1-arylethanol

Table 3 Iron oxide catalyzed cross-coupling reaction of organometallic species with 2-methyl THF *via* activation of α-C(sp^3)-H



1 **1**

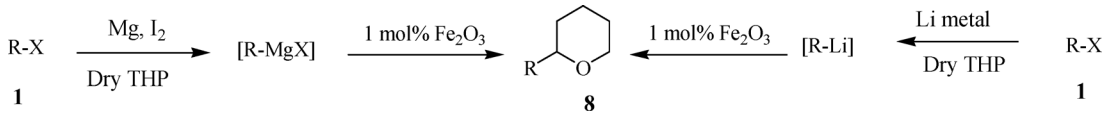
Entry	RMgX/RLi	6	7	Time (h)	Yield (%)[a]	Ratio(**6** : **7**%)[b]
a				3	58	40 : 60
b				3	60	51 : 49
c				3	55	42 : 58
d				4	57	38 : 62
e				3	58	41 : 59
f				3	59	51 : 49
g				3	53	40 : 60
h				4	55	38 : 62

All reactions carried out in 2-methyl tetrahydrofuran (2-MTHF) in the presence of Fe_20_3 (1 mol%),[a] Isolated yield, [b] Relative % was determined by ^{1}H NMR and GCMS.

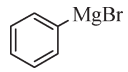
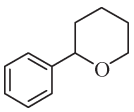
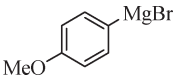
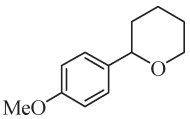
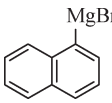
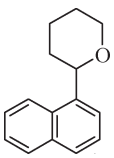
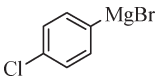
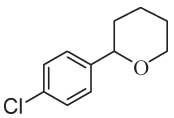
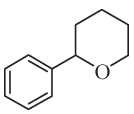
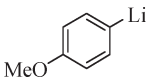
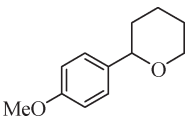
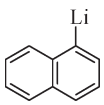
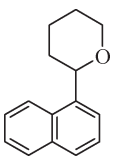
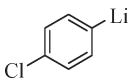
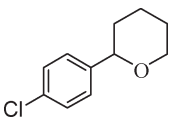
was also observed even without the catalyst *i.e.*, Fe_2O_3, which was formed by the cleavage of diethyl ether on reaction with organometallic species.[15]

The exact mechanism of this remarkable C–C bond formation is ambiguous, but previous reports proposed a radical process for iron mediated C–C cross-coupling reactions.[16] We speculate the involvement of radical intermediates and a plausible mechanism can be visualized through the addition of organometallic species on iron oxide, leading to the generation of organoiron species followed by abstraction of a proton from the 2-position of tetrahydrofuran to produce the 2-tetrahydrofuranyl radical. These radical and organometallic species could then be coupled directly to generate 2-phenyltetrahydrofuran **2a**. The formation of the phenol **4** and bis-phenol **5** byproducts may suggest intervention of unstable radicals or organoiron intermediates. However, the reaction of the allyl substrate was sluggish (Table 2, entry v) and the desired product was obtained in very low yield along with a mixture of unidentified products suggesting a radical mechanism. Further, the reaction of organometallic species with 2-MTHF gave the more branched product **7** also suggest the intervention of a radical mechanism. The results of the present methodology suggest that Fe_2O_3-based intermediates help the generation of carbon radicals and provide d-block organometallic surfaces for cross-coupling. This reaction provides new opportunities to prepare α-substituted furan and pyran drug-like scaffolds and analogues.

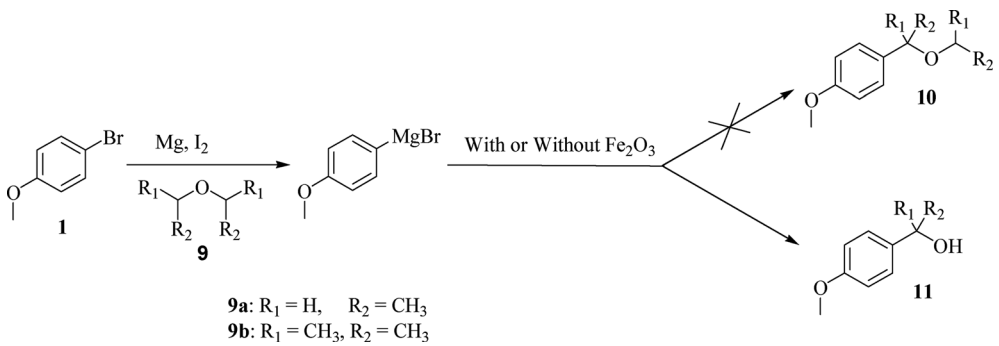
Table 4 Iron oxide catalyzed cross-coupling reaction of organometallic species with THP *via* activation of α-C(sp^3)-H



1 **8** **1**

Entry	RMgX/RLi	**8**	Time (h)	Yield (%)[a]
a			3	94
b			3	96
c			3	85
d			4	89
e			3	85
f			3	90
g			3	81
h			4	78

All reactions carried out in THP in the presence of Fe_20_3 (1 mol%),[a] Isolated yield.



Scheme 2 Studies towards the cross-coupling of arylmagnesium bromide with various acyclic ethers.

Conclusion

In summary, we have discovered a new method for the cross-coupling of organometallic species with cyclic unbranched and branched aliphatic ethers *via* the activation of α-C(sp^3)-H bond using Fe_2O_3. This Fe_2O_3 catalysed cross-coupling reaction is very selective towards cyclic ethers. No toxic or/and expensive ligands are required for this metallic catalysis. Further studies on the mechanism of this new method as well as an attempt towards the regioselective/stereoselectivity of this reaction are currently underway.

Experimental section

General

All reactions were performed under nitrogen/argon atmosphere. Analytical thin layer chromatography was performed using TLC pre-coated silica gel 60 F_{254} MERCK (20 × 20 cm). TLC plates were visualized by exposing UV light or by iodine vapours or immersion in an acidic staining solution of *p*-anisaldehyde followed by heating on a hot plate. Organic solutions were concentrated by rotary evaporation on a BUCHI-Switzerland R-120 rotary evaporator and vacuum pump V-710. Flash column chromatography was performed on Merck flash silica gel, 230–400 mesh size. Melting points of solid compounds were determined on BUCHI-B-545-Switzerland melting point apparatus. ^{1}H and ^{13}C NMR/DEPT spectra were recorded with BRUKER 500 and 400 MHz NMR instruments. Chemical data for protons are reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to the residual proton in the NMR solvent ($CDCl_3$: δ 7.26, or other solvents as mentioned). Carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded at 125 MHz or 100 MHz: chemical data for carbons are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to the carbon resonance of the solvent ($CDCl_3$: δ 77.0, or other solvents as mentioned). All the NMR spectra were processed in either MestReNova or Bruker software. Mass spectra were recorded with a VARIAN GC-MS-MS instrument. For HPLC, an LC 1100 (Agilent Technologies) instrument equipped with binary pump was used. The samples were analyzed on a Si-60 column (Merck, 5 μm, 4 × 250 mm) using an eluent {hexane: isopropyl alcohol (80 : 20)} with flow rate 0.5 ml min^{-1}, at the temperature 30 °C and with detector wavelength 210 nm.

Magnesium turnings were activated by 5% HCl solution and washed with distilled water five to ten times followed by methanol, acetone, and finally with diethylether and then dried under vacuum. HPLC grade tetrahydrofuran was dried by using sodium metal pressed strips and benzophenone under nitrogen atmosphere.

General procedure for cross-coupling of organometallic species with THF

In an oven dried flask, dried halo group-containing compounds (10 mmol) were added to dry THF containing magnesium or lithium (15 mmol, with a catalytic amount of iodine in the case of magnesium) at 0 °C. The whole reaction mixture was stirred vigorously until Grignard generation occurred. The reaction mixture was stirred at rt for an additional one hour. The resulting mixture was then added dropwise to a solution containing 1 mol % of ferric oxide in dry THF at 0 °C and stirred at rt while the progress of the reaction was monitored by TLC. After completion, saturated NH_4Cl solution was added and the reaction mixture was extracted with ethyl acetate (3 × 25 ml). The organic layer was dried over sodium sulphate. The volatiles were removed *in vaccuo*. The resultant compounds were purified on flash silica gel column chromatography using hexane/EtOAc as eluent. Pure compounds were analyzed by NMR (^{1}H/^{13}C/DEPT) and mass spectroscopy.

Tetrahydro-2-phenylfuran (Table 2, entry a, b and n). Colorless liquid TLC (EtOAc : hexane 3 : 7): R_f 0.35; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.60–1.69 (m, 2H), 1.70–1.87 (m, 2H), 3.61–3.72 (m, 2H), 4.70–4.72 (t, 1H, J = 6.3 Hz), 7.25–7.34 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): 29.14 (CH_2, C-4), 36.31 (CH_2, C-3), 62.70 (CH_2, C-5), 74.27 (CH, C-2), 125.80 (C-Ar), 127.42 (C-Ar), 128.41 (C-Ar), 144.70 (C-Ar); GC MS (EI) m\z (relative intensity): 148.2 (M^+, 9.8), 147.2 (12.5), 107.1 (76.0), 105.2 (24.6), 91 (13.7), 79.2 (99.9), 77.2 (46.2).

Tetrahydro-2-(4-methoxyphenyl)-furan (Table 2, entry c, d and o). White solid; m.p. = 61–63 °C TLC (EtOAc : hexane 3 : 7): R_f 0.25; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.58–1.75 (m, 2H), 1.78–1.91 (m, 2H), 3.62–3.73 (m, 2H), 3.80 (s, 3H), 4.66–4.70 (dd, 1H J = 5.5 & 7.2 Hz), 6.87–6.88 (d, 2H, J = 8.0 Hz), 7.27–7.29 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 29.12 (CH_2, C-4), 36.10 (CH_2, C-3), 55.25 (OCH_3), 62.48 (CH_2, C-5), 73.72 (CH, C-2), 113.72 (C-Ar), 127.06 (C-Ar), 136.95 (C-Ar), 158.80 (C-Ar); GC MS (EI) m\z (relative intensity): 178.1 (M^+, 25.2), 177.2 (32.9), 161.2 (22.0), 147.2 (34.3), 137.2 (99.9), 135.3 (56.7), 121.3 (10.7), 109.3 (50.6), 94.1 (28.7), 91.1 (16.3), 77.1 (33.3).

Tetrahydro-2-(2-methoxyphenyl)-furan (Table 2, entry e). Brownish liquid TLC (EtOAc : hexane 3 : 7): R_f 0.38; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.63–1.85 (m, 2H), 1.86–1.98 (m, 2H), 3.60–3.70 (m, 2H), 3.83 (s, 3H), 4.92–4.95 (t, 1H, J = 5.1), 6.87–6.98 (m, 2H), 7.24–7.26 (m, 1H), 7.32–7.34 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 29.50 (CH_2, C-4), 34.28 (CH_2, C-3), 55.29 (OCH_3), 62.88 (CH_2, C-5), 70.28 (CH, C-2), 110.60 (C-Ar), 120.76 (C-Ar), 126.72 (C-Ar), 128.26 (C-Ar), 132.43 (C-Ar), 156.28 (C-Ar); GC MS (EI) m\z (relative intensity): 178.1 (M^+, 25.2), 177.2 (32.9), 161.2 (22.0), 147.2 (34.3), 137.2 (99.9), 135.3 (56.7), 134.1 (9.9), 121.3 (10.7), 109.3 (50.6), 94.1 (28.7), 91.1 (16.3), 77.1 (33.3).

Tetrahydro-2-(3-methoxyphenyl)-furan (Table 2, entry f). White solid; m.p. = 62–64 °C TLC (EtOAc : hexane 3 : 7): R_f 0.31; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.64–1.75 (m, 2H), 1.83–1.88 (m, 2H), 3.64–3.81 (m, 2H), 3.81 (s, 3H), 4.69–4.72 (t, 1H, J = 6.3 Hz), 6.80–6.82 (m, 1H), 6.92–6.93 (m, 2H), 7.24–7.29 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 29.15 (CH_2, C-4), 36.27 (CH_2, C-3), 55.23 (OCH_3), 62.75 (CH_2, C-5), 74.20 (CH, C-2), 111.33 (C-Ar), 112.81 (C-Ar), 118.28 (C-Ar), 129.44 (C-Ar), 146.50 (C-Ar), 159.68 (C-Ar); GC MS (EI) m\z (relative intensity): 178.0 (M^+, 10.4), 161.0 (20.4), 137.0 (99.9), 135.1

(20.9), 121.0 (18.4), 107.0 (87.3), 93.9 (10.4), 90.9 (17.4), 79.0 (17.7), 77.0 (26.5).

Tetrahydro-2-*p*-tolylfuran (Table 2, entry g and p). Brownish liquid TLC (EtOAc : hexane 3 : 7): R_f 0.38; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.57–1.72 (m, 2H), 1.78–1.87 (m, 2H), 2.33 (s, 3H), 3.60–3.69 (m, 2H), 4.65–4.68 (t, 1H, J = 6.3 Hz), 7.13–7.15 (d, 2H, J = 7.8 Hz), 7.21–7.23 (d, 2H, J = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 21.07 (CH_3), 29.12 (CH_2, C-4), 36.17 (CH_2, C-3), 62.52 (CH_2, C-5), 73.99 (CH, C-2), 125.78 (C-Ar), 129.01 (C-Ar), 136.91 (C-Ar), 141.77 (C-Ar); GC MS (EI) m\z (relative intensity): 162.1 (M^+, 5.9), 147.2 (25.3), 145.2 (99.9), 121.2 (78.2), 119.2 (20.2), 93.1 (62.0), 91.1 (59.8), 77.2 (21.9), 71.2 (17.9).

2-(4-*tert*-Butylphenyl)-tetrahydrofuran (Table 2, entry h and q). White solid; m.p. = 72–74 °C TLC (EtOAc : hexane 3 : 7): R_f 0.41; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.32 (s, 9H), 1.63–1.69 (m, 2H), 1.70–1.91 (m, 2H), 3.65–3.74 (m, 2H), 4.70–4.73 (t, 1H, J = 6.3 Hz), 7.28–7.30 (d, 2H, J = 8.0 Hz), 7.36–7.38 (d, 2H, J = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): 29.25 (CH_2, C-4), 31.36 (CH_3 of ^{t}Bu), 34.40 (C of ^{t}Bu), 36.11 (CH_2, C-3), 62.73 (CH_2, C-5), 74.12 (CH, C-2), 125.30 (C-Ar), 125.53 (C-Ar), 141.62 (C-Ar), 150.37 (C-Ar); GC MS (EI) m\z (relative intensity): 203.2 (M^+, 5.2), 165.2 (13.8), 164.2 (14.1), 163.2 (99.9), 161.3 (10.3), 147.3 (67.2), 133.3 (15.5), 115.3 (12.2), 91.1 (34.6), 79.1 (14.8), 77.1 (14.6), 57.1 (40.5).

2-(4-Chlorophenyl)-tetrahydrofuran (Table 2, entry i). Colorless liquid TLC (EtOAc : hexane 3 : 7): R_f 0.32; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.63–1.73 (m, 2H), 1.79–1.88 (m, 2H), 3.64–3.74 (m, 2H), 4.70–4.73 (t, 1H, J = 5.8 Hz), 7.26–7.30 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): 28.83 (CH_2, C-4), 36.3 (CH_2, C-3), 62.31 (CH_2, C-5), 73.32 (CH, C-2), 127.19 (C-Ar), 128.45 (C-Ar), 132.89 (C-Ar), 143.16 (C-Ar); GC MS (EI) m\z (relative intensity): 183.1 (M^+, 3.6), 165.1 (25.0), 147.2 (14.4), 143.1 (29.6), 141.2 (99.9), 139.3 (19.5), 115.2 (19.8), 113.2 (38.5), 77.1 (90.4).

2-(3-Chlorophenyl)-tetrahydrofuran (Table 2, entry j). Colorless liquid TLC (EtOAc : hexane 3 : 7): R_f 0.32; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.64–1.72 (m, 2H), 1.81–1.88 (m, 2H), 3.65–3.74 (m, 2H), 4.70–4.73 (dd, J = 5.0 & 7.4 Hz, 1H), 7.21–7.36 (m, 3H), 7.37 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 28.85 (CH_2, C-4), 36.40 (CH_2, C-3), 62.51 (CH_2, C-5), 73.45 (CH, C-2), 123.96 (C-Ar), 125.96 (C-Ar), 127.40 (C-Ar), 129.66 (C-Ar), 134.20 (C-Ar), 146.86 (C-Ar); GC MS (EI) m\z (relative intensity): 183.0 (M^+, 13.6), 181.0 (39.5), 165.0 (12.1), 141.0 (10.2), 129.1 (10), 113.0 (10.8), 111 (4.9), 77.0 (28.8), 71.1 (99.9), 41.0 (10.8).

2-(3, 5-Difluorophenyl)-tetrahydrofuran (Table 2, entry k). Brownish liquid TLC (EtOAc : hexane 3 : 7): R_f 0.32; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.66–1.70 (m, 2H), 1.74–1.89 (m, 2H), 3.63–3.73 (m, 2H), 4.68–4.70 (t, 1H, J = 4.3 Hz), 6.66–6.70 (m, 1H), 6.86–6.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 28.61 (CH_2, C-4), 36.23 (CH_2, C-3), 62.33 (CH_2, C-5), 73.02 (CH, C-2), 102.46 (C-Ar), 108.43 (C-Ar), 108.681 (C-Ar), 149.06 (C-Ar), 161.84 (C-Ar), 164.14 (C-Ar); GC MS (EI) m\z (relative intensity): 185.0 (M^+, 23.2), 184.1 (14.4), 168.1 (10.1), 167.1 (99.9), 143.1 (13.6), 141.1 (11.6), 115.1 (36.6), 95.0 (8.9).

Tetrahydro-2-(naphthalen-4-yl)-furan (Table 2, entry l). White solid; m.p. = 98–100 °C TLC (EtOAc : hexane 3 : 7): R_f 0.41; ^{1}H NMR (500 MHz, CD_3OD): δ 1.54–2.01 (br m, 4H), 3.58 (br m, 2H), 5.46 (br m, 1H), 7.46–7.50 (br m, 3H), 7.64–7.66 (m, 1H), 7.75–7.77 (m, 1H), 7.85–7.87 (m, 1H), 8.13–8.14 (m, 1H); ^{13}C NMR (125 MHz, CD_3OD): 30.30 (CH_2, C-4), 36.17 (CH_2, C-3), 62.93 (CH_2, C-5), 71.38 (CH, C-2), 123.95 (C-Ar), 124.33 (C-Ar), 126.40 (C-Ar), 126.42 (C-Ar), 126.84 (C-Ar), 128.59 (C-Ar), 129.83 (C-Ar), 131.87 (C-Ar), 135.34 (C-Ar), 142.14 (C-Ar); GC MS (EI) m\z (relative intensity): 227.0 (99.9), 197.0 (M^+, 10.2), 195.0 (24.5), 183.0 (11.1), 181.0 (13.1), 165.0 (16.4), 152.0 (13.1), 137.0 (12.1), 135.0 (92.4), 121.0 (34.0), 109.0 (23.4), 108.0 (76.9), 77.0 (46.0).

2-(5-methylthiophen-2-yl)-tetrahydrofuran (Table 2, entry m). Brownish liquid TLC (EtOAc : hexane 3 : 7): R_f 0.41; ^{1}H NMR (500 MHz, $CDCl_3$): 1.57–1.72 (m, 2H), 1.83–1.91 (m, 2H), 2.47 (s, 3H), 3.68–3.72 (m, 2H), 4.72–4.74 (m, 1H), 6.74 (s, 1H), 6.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 15.36 (CH_3), 28.97 (CH_2, C-4), 35.32 (CH_2, C-3), 62.62 (CH_2, C-5), 70.51 (CH, C-2), 118.30 (C-Ar of thiophene), 123.92 (C-Ar of thiophene), 140.40 (C-Ar of thiophene), 145.90 (C-Ar of thiophene); GC MS (EI) m\z (relative intensity): 168.0 (M^+, 17.4), 140.0 (17.4), 127.0 (46.5), 111.1 (18.1), 99.0(99.9), 77.1 (6.5), 65.1 (29.7), 59.0 (9.8).

Tetrahydro-2-octylfuran (Table 2, entry r). Colorless liquid TLC (EtOAc : hexane 3 : 7): R_f 0.38; ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.86–0.91 (m, 3H), 1.26–1.33 (br m, 14H), 1.53–1.58 (m, 2H), 1.67–1.78 (m, 2H), 3.62–3.64 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 14.13 (CH_3), 22.70 (CH_2), 25.76 (CH_2), 29.14 (CH_2), 29.37 (CH_2), 29.63 (CH_2), 29.68 (CH_2), 31.93 (CH_2), 34.35 (CH_2), 37.65 (CH_2, C-3), 63.09 (CH_2, C-5), 71.97 (CH, C-2); GC MS (EI) m\z (relative intensity): 97.1 (52), 85.1 (38.4), 71.2 (63.7), 57.2 (99.9), 43.2 (13.2).

2-Dodecyl-tetrahydrofuran (Table 2, entry s). Colorless liquid TLC (EtOAc : hexane 3 : 7): R_f 0.39; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86–0.90 (m, 3H), 1.26–1.31 (br m, 22H), 1.46–1.71 (m, 4H), 3.62–3.64 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 14.12 (CH_3), 22.70 (CH_2), 25.76 (CH_2), 29.16 (CH_2), 29.36 (CH_2), 29.45 (CH_2), 29.62 to 29.71 (multiple peaks of CH_2), 31.93 (CH_2), 32.83 (CH_2), 34.36 (CH_2), 37.68 (CH_2, C-3), 63.11 (CH_2, C-5), 71.96 (CH, C-2); GC MS (EI) m\z (relative intensity): 85.0 (22.3), 71.1 (49.8), 70.2 (17.2), 57.2 (99.9), 56.2 (17.4), 55.2 (18.7), 42.2 (53.7), 41.2 (58.5).

Tetrahydro-2-tetradecylfuran (Table 2, entry t). White solid; m.p. = 54–56 °C TLC (EtOAc : hexane 3 : 7): R_f 0.39; ^{1}H NMR (500 MHz $CDCl_3$): δ 0.91–0.93 (m, 3H), 1.29 (br m, 22H), 1.45–1.53 (m, 4H), 1.55–1.77 (m, 4H), 3.68–3.77 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.13 (CH_3), 22.70 (CH_2), 25.74 (CH_2), 29.14 (CH_2), 29.37 (CH_2), 29.61 to 29.71 (multiple peaks of CH_2), 31.94 (CH_2), 34.35 (CH_2), 37.65 (CH_2, C-3), 63.10 (CH_2, C-5), 71.97 (CH, C-2); GC MS (EI) m\z (relative intensity): 151.0 (10.9), 137.0 (97.7), 135.1 (99.9), 97.0 (11.0), 85.0 (28.2), 71.1 (52.2), 69.1 (44.1), 57.1 (93.4), 55.1 (63.9).

2-*sec*-Butyl-tetrahydrofuran (Table 2, entry u). Brownish liquid TLC (EtOAc : hexane 3 : 7): R_f 0.36; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 0.88–0.93 (m, 6H), 1.19–1.25 (m, 2H), 1.45–1.73

(m, 4H, signal obscured with moisture peak), 2.10–2.37 (m, 1H), 3.47–3.58 (m, 1H), 3.64–3.75 (m, 2H);^{13}C NMR (100 MHz $CDCl_3$): δ 11.64 (CH_3), 11.82 (CH_3), 13.46 (CH_3), 14.62 (CH_3), 24.82 (CH_2), 25.83 (CH_2), 29.56 (CH_2, C-4), 29.81 (CH_2, C-4), 30.36 (CH_2, C-3), 31.43 (CH_2, C-3), 40.44 (CH), 40.69 (CH), 62.96 (CH_2, C-5), 63.00 (CH_2, C-5), 75.08 (CH, C-2), 75.72 (CH, C-2); GC MS (EI) m\z (relative intensity): 127.2 (19.8), 95.2 (29.3), 84.2 (11.1), 82.2 (10.9), 71.2 (57.2), 69.3 (21.2), 67.3 (21.8), 61.2 (15.0), 43.1 (99.9), 41.2 (85.0).

General procedure for cross-coupling of organometallic species with 2-methyl THF

In an oven dried flask, dried halo group-containing compounds (10 mmol) were added in dry 2-methyl THF containing magnesium or lithium (15 mmol, catalytic amount of iodine in case of magnesium) at 0 °C. The whole reaction mixture was stirred vigorously until organometallic species generation occurred. The reaction mixture was stirred at rt for an additional one hour. The resulting mixture was then added dropwise to a solution containing 1 mol% ferric oxide in dry 2-methyl THF at 0 °C and then allowed to stir at rt, the progress of the reaction was monitored by TLC. After completion, saturated NH_4Cl solution was added and the reaction mixture was extracted with ethyl acetate (3 × 25 ml). The organic layer was dried over sodium sulphate. The volatiles were removed *in vaccuo*. The resultant compounds were purified on flash silica gel column chromatography using hexane/EtOAc as the eluent. Pure compounds were analyzed by NMR (^{1}H/^{13}C/DEPT) and mass spectroscopy.

2-Methyl-5-phenyl-tetrahydrofuran (6a/e) and 2-methyl-2-phenyl-tetrahydrofuran (7a/e) (Table 3, entries a and e). Brownish liquid TLC (EtOAc: hexane 3 : 7): R_f 0.37; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.18–1.20 (d, CH_3 of **6a**/**e**), 1.47–1.53 (m, CH_2 of 2-MTHF), 1.57 (s, 3H of **7a**/**e**), 1.80–2.05 (m, CH_2 of 2-MTHF), 3.55–3.65 (m, 2H of **7a**/**e**), 3.82–3.89 (m, CH of **6a**/**e**), 4.68–4.75 (m, CH of **6a**/**e**), 7.21–7.44 (m, aromatic protons); ^{13}C NMR (100 MHz, $CDCl_3$): 23.04 (CH_3, **6a**/**e**), 23.39 (CH_3, **6a**/**e**), 26.97 (CH_2, C-4, **7a**/**e**), 30.28 (CH_3, **7a**/**e**), 34.69 (CH_2, C-3, **6a**/**e**), 34.88 (CH_2, C-3, **6a**/**e**), 35.78 (CH_2, C-4, **6a**/**e**), 36.01 (CH_2, C-4, **6a**/**e**), 40.89 (CH_2, C-3, **7a**/**e**), 62.49 (CH_2, C-5, **7a**/**e**), 67.47 (CH, C-5, **6a**/**e**), 67.98 (CH, C-5, **6a**/**e**), 73.83 (CH, C-2, **6a**/**e**), 74.18 (C, C-2, **7a**/**e**), 74.39 (CH, C-2, **6a**/**e**), 124.85 (C-Ar), 125.85 (C-Ar), 125.87 (C-Ar), 126.28 (C-Ar), 127.16 (C-Ar), 127.21 (C-Ar), 128.01 (C-Ar), 128.24 (C-Ar), 128.26 (C-Ar), 144.67 (C-Ar), 144.87 (C-Ar), 148.00 (C-Ar); GC MS for **6a**/**e** (EI) m\z (relative intensity): 162.2 (M^+, 21.7), 145.3 (53.3), 117.3 (27.7), 107.3 (63.2), 91.1 (20.8), 85.2 (7.5), 79.2 (99.9), 77.2 (64.4), 43.2 (15.6); for **7a**/**e**: 163.2 (M+1, 28.2), 147.2 (50.6), 146.3 (11.9), 145.3 (99.9), 121.3 (67.5), 117.4 (11.7), 105.3 (53.0), 91.2 (14.1), 77.2 (26.1), 51.1 (6.8), 43.1 (52.0).

2-(4-Methoxyphenyl)-5-methyl-tetrahydrofuran (6b/f) and 2-(4-methoxyphenyl)-2-methyl-tetrahydrofuran (7b/f) (Table 3, entries b and f). Brownish liquid TLC (EtOAc : hexane 3 : 7): R_f 0.28; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.17–1.19 (d, CH_3 of **6b**/**f**), 1.46–1.58 (m, CH_2 of 2-MTHF and CH_3 of **7b**/**f**), 1.83–1.98 (m, CH_2 of 2-MTHF), 3.57–3.61 (m, 2H of **7b**/**f**), 3.80–3.89 (m, CH of **6b**/**f** and OCH_3 of both **6b**/**f** and **7b**/**f**), 4.62–4.69 (m, CH of **6b**/**f**), 6.85–7.35 (m, aromatic protons); ^{13}C NMR (100 MHz, $CDCl_3$): 23.18 (CH_3, **6b**/**f**), 23.51 (CH_3, **6b**/**f**), 27.16 (CH_2, C-4, **7b**/**f**), 30.40 (CH_3, **7b**/**f**), 34.90 (CH_2, C-3, **6b**/**f**), 34.92 (CH_2, C-3, 6**b**/**f**), 35.96 (CH_2, C-4, **6b**/**f**), 36.03 (CH_2, C-4, **6b**/**f**), 41.08 (CH_2, C-3, **7b**/**f**), 55.21 (OCH_3), 55.24 (OCH_3), 55.35 (OCH_3), 62.69 (CH_2, C-5, **7b**/**f**), 67.54 (CH, C-5, **6b**/**f**), 68.06 (CH, C-5, **6b**/**f**), 73.59 (CH, C-2, **6b**/**f**), 73.93 (C, C-2, **7b**/**f**), 74.11 (CH, C-2, **6b**/**f**), 111.40 (C-Ar), 113.38 (C-Ar), 113.71 (C-Ar), 120.90 (C-Ar), 126.05 (C-Ar), 126.80 (C-Ar), 127.06 (C-Ar), 127.09 (C-Ar), 128.10 (C-Ar), 136.96 (C-Ar), 137.17 (C-Ar), 140.30 (C-Ar), 156.60 (C-Ar), 158.00 (C-Ar), 158.76 (C-Ar); GC MS for **6b**/**f** (EI) m\z (relative intensity): 191.1 (M-1, 29.4), 177.1 (12.7), 175.2 (45.0), 150.2 (10.0), 147.2 (21.6), 135.3 (99.9), 134.4 (32.2), 121.3 (16.0), 109.3 (38.5), 107.3 (7.1), 91.1 (21.3), 77.1 (33.9), 78.1 (13.4), 43.0 (8.0); for **7b**/**f**: 193.1 (M+1, 13.1), 177.1 (99.9), 175.3 (11.6), 151.2 (30.9), 148.3 (18.4), 135.3 (81.9), 115.3 (6.2), 92.0 (6.6), 77.1 (18.3), 63.1 (6.3), 43.0 (18.1).

2-Methyl-5-(naphthalen-1-yl)-tetrahydrofuran (6c/g) and 2-methyl-2-(naphthalen-1-yl)-tetrahydrofuran (7c/g) (Table 3, entries c and g). White solid; m.p. = 110 °C TLC (EtOAc: hexane 3 : 7): R_f 0.42; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20–1.21 (d, CH_3 of **6c**/**g**), 1.43–1.71 (m, CH_2 of 2-MTHF), 1.84 (s, 3H of **7c**/**g**), 2.14–2.46 (m, CH_2 of 2-MTHF), 3.56–3.59 (m, 2H of **7c**/**g**), 3.87–3.95 (m, CH of **6c**/**g**), 5.47–5.54 (m, CH of **6c**/**g**), 7.39–8.66 (m, aromatic protons); ^{13}C NMR (100 MHz, $CDCl_3$): 23.15 (CH_3, **6c**/**g**), 23.52 (CH_3, **6c**/**g**), 27.52 (CH_2, C-4, **7c**/**g**), 29.80 (CH_3, **7c**/**g**), 34.20 (CH_2, C-3, **6c**/**g**), 35.02 (CH_2, C-3, **6c**/**g**), 35.45 (CH_2, C-4, **6c**/**g**), 36.22 (CH_2, C-4, **6c**/**g**), 39.58 (CH_2, C-3, **7c**/**g**), 62.58 (CH_2, C-5, **7c**/**g**), 67.67 (CH, C-5, **6c**/**g**), 68.13 (CH, C-5, **6c**/**g**), 70.47 (CH, C-2, **6c**/**g**), 71.06 (CH, C-2, **6c**/**g**), 75.81 (C, C-2, **7c**/**g**), 122.88 (C-Ar), 123.07 (C-Ar), 123.22 (C-Ar), 123.90 (C-Ar), 124.97 (C-Ar), 125.07 (C-Ar), 125.26 (C-Ar), 125.46 (C-Ar), 125.52 (C-Ar), 125.94 (C-Ar), 126.78 (C-Ar), 127.64 (C-Ar), 128.36 (C-Ar), 128.92 (C-Ar), 129.24 (C-Ar), 130.35 (C-Ar), 130.84 (C-Ar), 133.80 (C-Ar), 134.89 (C-Ar), 140.46 (C-Ar), 140.70 (C-Ar), 142.83 (C-Ar); GC MS for **6c**/**g** (EI) m\z (relative intensity): 212 (M^+, 26.5), 197.1 (17.9), 195.1 (9.7), 167.2 (18.5), 157.2 (66.5), 155.3 (51.6), 153.4 (32.0), 152.4 (24.9), 141.3 (16.4), 129.3 (99.9), 127.4 (39.0), 115.4 (13.0), 77.1 (7.9), 43.0 (14.9); for **7c**/**g**: 212 (M^+, 16.4), 197.1 (99.9), 178.2 (10.7), 167.3 (21.7), 166.3 (37.9), 165.3 (56.9), 155.3 (86.0), 128.3 (25.1), 127.3 (54.9), 102.3 (5.4), 77.1 (8.6), 43.0 (14.9).

2-(4-Chlorophenyl)-5-methyl-tetrahydrofuran (6d/h) and 2-(4-chlorophenyl)-2-methyl-tetrahydrofuran (7d/h) (Table 3, entries d and h). Brownish liquid TLC (EtOAc : hexane 3 : 7): R_f 0.34; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.16–1.17 (d, CH_3 of **6d**/**h**), 1.45–1.58 (m, CH_2 of 2-MTHF), 1.52 (s, 3H of **7d**/**h**), 1.80–2.00 (m, CH_2 of 2-MTHF), 3.56–3.60 (m, 2H of **7d**/**h**), 3.81–3.87 (m, CH of **6d**/**h**), 4.68–4.71 (m, CH of **6d**/**h**), 7.25–7.35 (m, aromatic protons); ^{13}C NMR (100 MHz, $CDCl_3$): 23.25 (CH_3, **6d**/**h**), 23.59 (CH_3, **6d**/**h**), 26.93 (CH_2, C-4, **7d**/**h**), 30.49 (CH_3, **7d**/**h**), 34.55 (CH_2, C-3, **6d**/**h**), 34.96 (CH_2, C-3, **6d**/**h**), 35.77 (CH_2, C-4, **6d**/h), 36.21 (CH_2, C-4, **6d**/**h**), 41.05 (CH_2, C-3, **7d**/**h**), 62.64 (CH_2, C-5, **7d**/**h**), 67.63 (CH, C-5,

6d/h), 68.16 (CH, C-5, **6d/h**), 73.24 (CH, C-2, **6d/h**), 73.86 (C, C-2, **7d/h**), 73.95 (CH, C-2, **6d/h**), 126.45 (C-Ar), 127.21 (C-Ar), 127.24 (C-Ar), 128.16 (C-Ar), 128.44 (C-Ar), 128.45 (C-Ar), 132.14 (C-Ar), 132.85 (C-Ar), 132.89 (C-Ar), 143.16 (C-Ar), 143.38 (C-Ar), 146.55 (C-Ar); GC MS for **6d/h** (EI) m\z (relative intensity): 197.1 (M+1, 18.5), 195.1 (7.4), 181.1 (14.1), 179.1 (20.8), 161.2 (24.9), 157.1 (6.4), 141.3 (92.7), 125.3 (12.4), 113.3 (42.9), 89.1 (8.0), 77.1 (99.9), 75.1 (14.8), 50.1 (7.7), 43.0 (16.9); for **7d/h**: 197.1 (M+1, 14.5), 182.1 (5.1), 181.1 (50.1), 179.3 (40.6), 157.2 (30.0), 155.3 (99.9), 154.5 (15.0), 152.5 (6.6), 139.4 (45.1), 125.4 (6.4), 111.3 (13.6), 75.1 (11.4), 51.1 (4.6).

General procedure for cross-coupling of organometallic species with THP

In an oven dried flask, dried halo group-containing compounds (10 mmol) were added in dry THP containing magnesium or lithium (15 mmol, catalytic amount of iodine in case of magnesium) at 0 °C. The whole reaction mixture was stirred vigorously until organometallic species generation occurred. The reaction mixture stirred at rt for an additional one hour. The resulting mixture was then added dropwise to a solution containing 1 mol% of ferric oxide in dry THP at 0 °C and then allowed the resulting reaction mixture to stir at rt and progress of the reaction was monitored by TLC. After completion, saturated NH_4Cl solution was added and the reaction mixture was extracted with ethyl acetate (3 × 25 ml). The organic layer was dried over sodium sulphate. The volatiles were removed *in vaccuo*. The resulting compounds were purified by flash silica gel column chromatography using hexane/EtOAc as an eluent. Pure compounds were analyzed by NMR ($^1H/^{13}C$/DEPT) and mass spectroscopy.

2-Phenyl-tetrahydro-2*H*-pyran (Table 4, entries a and e). Brownish liquid TLC (EtOAc : hexane 3 : 7): R_f 0.36; ^1H NMR (400 MHz, $CDCl_3$): δ 1.48–1.63 (m, 4H), 1.70–1.85 (m, 2H), 3.60–3.63 (t, 2H, J = 6.3 Hz), 4.66–4.69 (t, 1H, J = 6.5 Hz), 7.26–7.35 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): 21.96 (CH_2, C-4), 32.27 (CH_2, C-5), 38.64 (CH_2, C-3), 62.35 (CH_2, C-6), 74.29 (CH, C-2), 125.83 (C-Ar), 127.39 (C-Ar), 128.37 (C-Ar), 144.85 (C-Ar); GC MS (EI) m\z (relative intensity): 162.1 (M^+, 5.6), 145.2 (29.7), 133.1 (5.4), 107.1 (85.5), 105.2 (16.4), 79.1 (99.9), 77.2 (42.7), 51.1 (7.0).

2-(4-Methoxyphenyl)-tetrahydro-2*H*-pyran (Table 4, entries b and f). Brownish liquid TLC (EtOAc : hexane 3 : 7): R_f 0.25; ^1H NMR (400 MHz, $CDCl_3$): δ 1.32–1.98 (m, 6H), 3.61–3.66 (m, 2H), 3.80 (s, 3H), 4.59–4.63 (m, 1H), 6.83–6.89 (d, 2H, J = 8.0 Hz), 7.26–7.29 (d, 2H, J = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): 22.02 (CH_2, C-4), 32.31 (CH_2, C-5), 38.54 (CH_2, C-3), 55.25 (OCH_3), 62.41 (CH_2, C-6), 73.92 (CH, C-2), 113.76 (C-Ar), 127.16 (C-Ar), 137.02 (C-Ar), 158.90 (C-Ar); GC MS (EI) m\z (relative intensity): 192.2 (M^+, 14.9), 161.2 (7.2), 137.2 (99.9), 135.3 (36.7), 122.3 (10.5), 109.32 (41.2), 94.1 (22.6), 78.1 (7.4).

2-(Naphthalen-4-yl)-tetrahydro-2*H*-pyran (Table 4, entries c and g). White solid; m.p. = 98–100 °C TLC (EtOAc : hexane 3 : 7): R_f 0.41; ^1H NMR (400 MHz, CD_3OD): δ 1.47–1.61 (m, 4H), 1.82–1.97 (m, 2H), 3.51–3.54 (t, 2H, J = 6.2 Hz), 5.42–5.45 (m, 1H), 7.44–7.52 (m, 3H), 7.63– 7.65 (d, 1H, J = 7.0 Hz), 7.75–7.77 (d, 1H, J = 8.2 Hz), 7.85–7.87 (d, 1H, J = 9.4 Hz), 8.12–8.14 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, CD_3OD): 23.57 (CH_2, C-4), 33.53 (CH_2, C-5), 39.50 (CH_2, C-3), 62.86 (CH_2, C-6), 71.50 (CH, C-2), 123.94 (C-Ar), 124.25 (C-Ar), 126.36 (C-Ar), 126.76 (C-Ar), 128.53 (C-Ar), 129.81 (C-Ar), 131.85 (C-Ar), 135.29 (C-Ar), 142.14 (C-Ar); GC MS (EI) m\z (relative intensity): 212.2 (M^+, 11.1), 195.2 (33.9), 158.2 (8.9), 129.3 (99.9).

2-(4-Chlorophenyl)-tetrahydro-2*H*-pyran (Table 4, entries d and h). Colorless liquid TLC (EtOAc : hexane 3 : 7): R_f 0.33; ^1H NMR (400 MHz, $CDCl_3$): δ 1.41–1.59 (m, 4H), 1.61–1.78 (m, 2H), 3.57–3.60 (t, 2H, J = 6.1 Hz), 4.60–4.64 (t, 1H, J = 5.8 Hz), 7.23–7.30 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): 21.89 (CH_2, C-4), 32.23 (CH_2, C-5), 38.69 (CH_2, C-3), 62.46 (CH_2, C-6), 73.65 (CH, C-2), 127.24 (C-Ar), 128.55 (C-Ar), 133.06 (C-Ar), 143.30 (C-Ar); GC MS (EI) m\z (relative intensity): 196.0 (M^+, 11.5), 179.2 (99.9), 141.2 (16.0), 113.2 (8.8), 77.1 (12.8).

General procedure for cross-coupling of organometallic species with acyclic ether

In an oven dried flask, dried halo group-containing compounds (10 mmol) were added in dry acyclic ether containing magnesium (15 mmol, catalytic amount of iodine) at 0 °C. The whole reaction mixture was stirred vigorously until Grignard generation occurred. The reaction mixture was stirred at room temperature for additional one hour. The resulting mixture was then added dropwise to a solution containing 1 mol% of ferric oxide in dry acyclic ether at 0 °C and then the resulting reaction mixture was allowed to stir at room temperature and the progress of the reaction was monitored by TLC. After completion, saturated NH_4Cl solution was added and the reaction mixture was extracted with ethyl acetate (3 × 25 ml). The organic layer was dried over sodium sulphate. The volatiles were removed *in vaccuo*. The resultant compounds were purified on flash silica gel column chromatography using hexane/EtOAc as an eluent. Pure compounds were analyzed by NMR ($^1H/^{13}C$/DEPT) and GCMS and identified as 1-(4-methoxyphenyl)-ethanol **11**.

1-(4-Methoxyphenyl)-ethanol (Scheme 2, entry 11). Colorless liquid TLC (EtOAc : hexane 3 : 7): R_f 0.21; ^1H NMR (400 MHz, $CDCl_3$): δ 1.47–1.49 (d, 3H, J = 6.4 Hz), 3.80 (s, 3H), 4.61–4.88 (q, 1H, J = 6.4 Hz), 6.77–6.90 (m, 2H), 7.26–7.32 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 24.99 (CH_3), 55.27 (OCH_3), 69.86 (CH), 113.81 (C-Ar), 126.69 (C-Ar), 138.06 (C-Ar), 158.89 (C-Ar); GC MS (EI) m\z (relative intensity): 152.0 (M^+, 19.5), 137.0 (99.9), 119.0 (33.5), 109.0 (82.7), 91.0 (55.5), 77.0 (39.9), 63.0 (18.3), 42.9 (8.9).

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