Iron-Catalysed, Hydride-Mediated Reductive Cross-Coupling of Vinyl Halides and Grignard Reagents

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General Experimental

All air and moisture sensitive manipulations were carried out using standard vacuum line and Schlenk techniques, or in a drybox containing a purified argon atmosphere. Solvents for air and moisture sensitive manipulations were obtained from an Anhydrous Engineering Solvent Purification System. All glassware was cleaned using base (KOH, ^{i}PrOH) then acid (HCl_{aq}) baths.

^{1}H, ^{13}C and ^{11}B NMR spectra were recorded on Varian VNMR 400 and 500MHz or Jeol Eclipse 300 and 400MHz spectrometers. All spectra were obtained at ambient temperature unless stated otherwise. All ^{1}H, ^{13}C NMR shifts are reported relative to tetramethylsilane as an internal standard and $CDCl_3$ unless otherwise stated, with ^{1}H (residual) and ^{13}C chemical shifts of the solvent as a secondary standard. The chemical shifts (δ) were recorded in parts per million (ppm) and the coupling constants (*J*) in Hertz (Hz). ^{1}H NMR multiplicity and coupling constants are reported where applicable.

Iron(II) chloride was purchased from Strem Chemicals Inc. (UK); anhydrous iron chloride, 98% (product number 93-2631. Lot 19226800, 44.0000% Fe, expect 44.06%). Borane dimethylamine complex was purchased from Sigma-Aldrich Co. (UK); Borane dimethylamine complex (product number 180238).

Catalytic reactions were assayed by gas-chromatography by comparison to authentic samples. Where full reduction did not occur, conversions were estimated by integration of relevant peak areas in GC-MS data. Gas chromatography was performed on two machines: an Agilent HP6890 gas chromatograph equipped with an Agilent J&W DB-5ms capillary column (15 m × 0.25 mm × 0.25 μm), or a Shimadzu GCMS-QP2010 equipped with a Varian SPSIL 5CB column (30 m x 0.25 mm x 0.25 μm). Several different methods were used:

[50-1]: Injector temp. 200 °C, 50 °C for 3 min, ramps 5 °Cmin^{-1} to 150 °C, ramps 45 °Cmin^{-1} to 250 °C, holds for 3 min, ramps 45 °Cmin^{-1} to 300 °C, holds for 3 min.

[50-SPT]: Injector temp. 200 °C, 50 °C for 3 min, ramps 5 °Cmin^{-1} to 80 °C, ramps 45 °Cmin^{-1} to 300 °C, holds for 2 min.

[TE Labs]: Injector temp. 300 °C, 50 °C for 1 min, ramps 10 °Cmin^{-1} to 300 °C, holds for 5 min.

Magnetic moments were measured using Evans NMR method (solvent, CD2Cl2; standard, ferrocene). Infra-red spectra were recorded on a Perkin-Elmer Spectrum One FT-IR spectrometer. High resolution mass spectra were recorded on a VG autospec mass spectrometer.

General Procedures

General procedure A: Ligand optimisation

β-Bromostyrene (0.13 mL, 1 mmol) was added to a solution of $FeCl_2$ (13 mg, 0.1 mmol) and ligand in anhydrous THF (10 mL) and the mixture cooled to -78 °C. The organomagnesium chloride (0.7 mL, 2 M in THF) was added dropwise and after 15 minutes sodium triethylborohydride (10 mL, 1 M in THF) was added dropwise. The reaction mixture was stirred for 16 hours, allowing the bath and reaction mixture to warm to room temperature over this time. Saturated aqueous NH_4Cl (10 mL) was added and the aqueous phase extracted with diethyl ether (3 x 10 mL). The combined organic extracts were washed with H_2O and brine, dried ($MgSO_4$) and concentrated *in vacuo* to give the crude reaction products.

All products were known, identified by GC-MS and ^1H NMR, and characterised by comparison with authentic samples of spectral data.

General procedure B: Optimisation of hydride and conditions

β-Bromostyrene (0.13 mL, 1 mmol) was added to a solution of iron catalyst [**9**$FeCl_2$] (42 mg, 0.1 mmol) in anhydrous THF (10 mL) and the mixture cooled to -20 °C. Ethylmagnesium chloride (0.7 mL, 2 M in THF) was added dropwise and after 15 minutes the hydride reagent (10 mmol) was added dropwise. The reaction mixture was stirred for 16 hours, allowing the bath and reaction mixture to warm to room temperature over this time. Saturated aqueous NH_4Cl (10 mL) was added and the aqueous phase was extracted with diethyl ether (3 x 10 mL). The combined organic extracts were washed with H_2O (10 mL) and brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give the crude reaction products.

All products were known, identified by GC-MS and ^1H NMR, and characterised by comparison with authentic samples of spectral data.

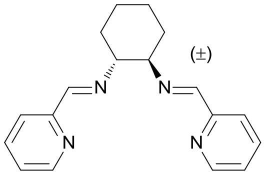
General procedure C: Reductive cross-coupling of *β*-aryl vinyl halides and Grignard reagents

The *β*-aryl vinyl halide was added to a solution of iron catalyst [**9**$FeCl_2$] (10 mol%) in anhydrous THF and the mixture cooled to -20 °C. The Grignard reagent (1.4 eq.) was added dropwise and after 15 minutes lithium dimethylaminoborohydride (10 eq.) was added dropwise. The reaction mixture was stirred for 16 hours, allowing the bath and reaction mixture to warm to room temperature over this time. The solution was concentrated *in vacuo* and re-dissolved in CH_2Cl_2. Aqueous HCl (10 mL, 1 M) was added and the mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL) and the combined organic extracts washed with H_2O (10 mL) and brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give the crude reaction products.

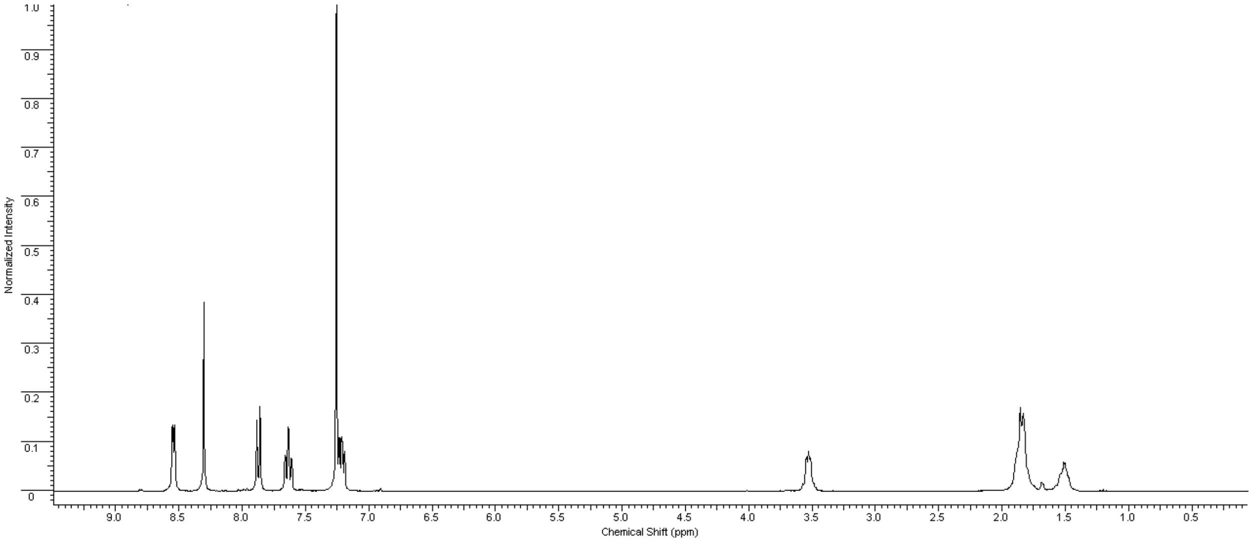
All products were known, identified by GC-MS and ^{1}H NMR, and characterised by comparison with authentic samples of spectral data.

In order to determine isolated yields, the crude reaction products were re-dissolved in CH_2Cl_2 (2 mL) and purified by flash column chromatography (100% pentane) to give the product. The samples were analysed by ^{1}H and ^{13}C NMR.

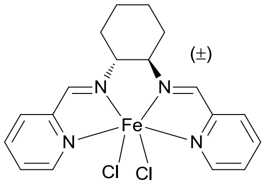
Preparation of (±)-(*N*,*N'*-bis(pyridin-2-ylmethylene)cyclohexane-1,2-diamine 9



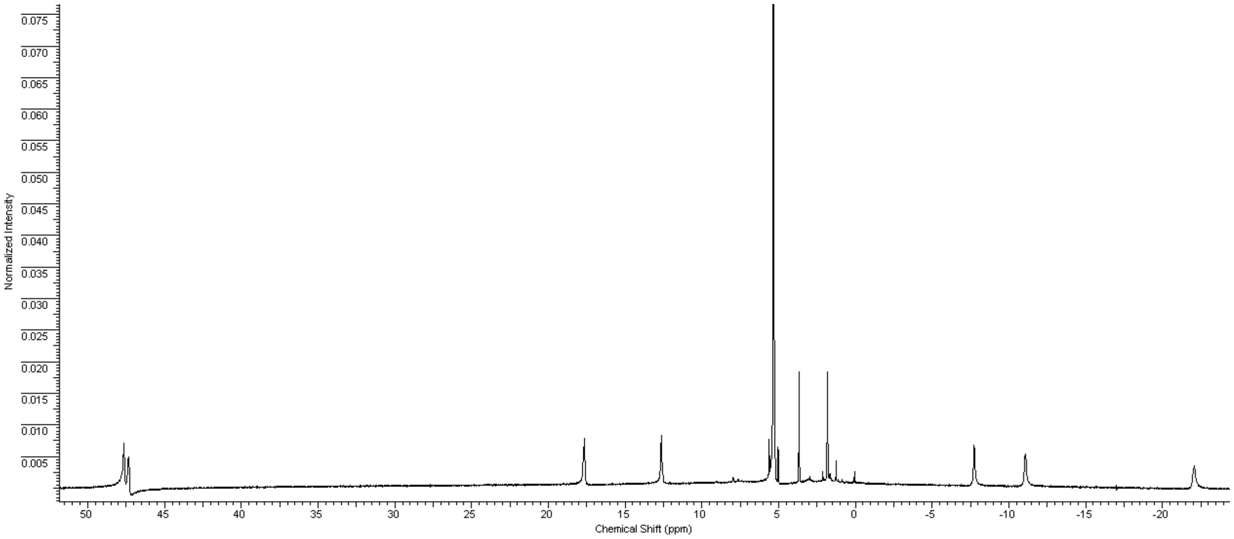
2-Pyridinecarboxaldehyde (0.84 mL, 8.8 mmol) in anhydrous methanol (20 mL) was added to a solution of (±)-*trans*-diaminocyclohexane (0.48 mL, 4 mmol) in anhydrous methanol (20 mL) and molecular sieves (3 Å) at 0 °C. The reaction mixture was stirred for 16 hours, allowing the bath and reaction mixture to warm to room temperature over this time. The solution was filtered through celite and the solvent removed *in vacuo* to give (±)-(*N*,*N'*-bis(pyridin-2-ylmethylene)cyclohexane-1,2-diamine **9** (1.1 g, 94 %) as yellow needles. δ_H (300 MHz, $CDCl_3$) 8.55 (2H, ddd, *J=5.0 Hz, 1.7 Hz, 0.9 Hz*), 8.32 (2H, s), 7.89 (2H, dt, *J=7.9 Hz, 1.0 Hz*), 7.65 (2H, dt, *J=7.6 Hz, 1.7 Hz*), 7.23 (2H, ddd, *J=7.5 Hz, 4.8 Hz, 1.3 Hz*), 3.50-3.59 (2H, m), 1.80-1.92 (6H, m), 1.47-1.57 (2H, m).[1]

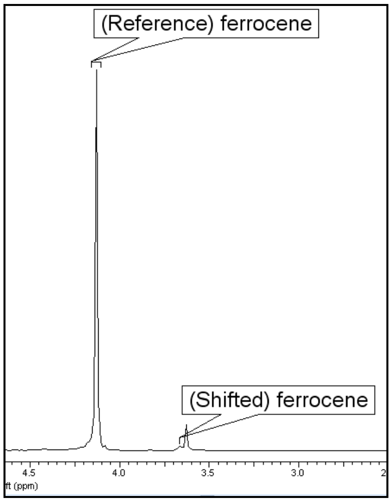


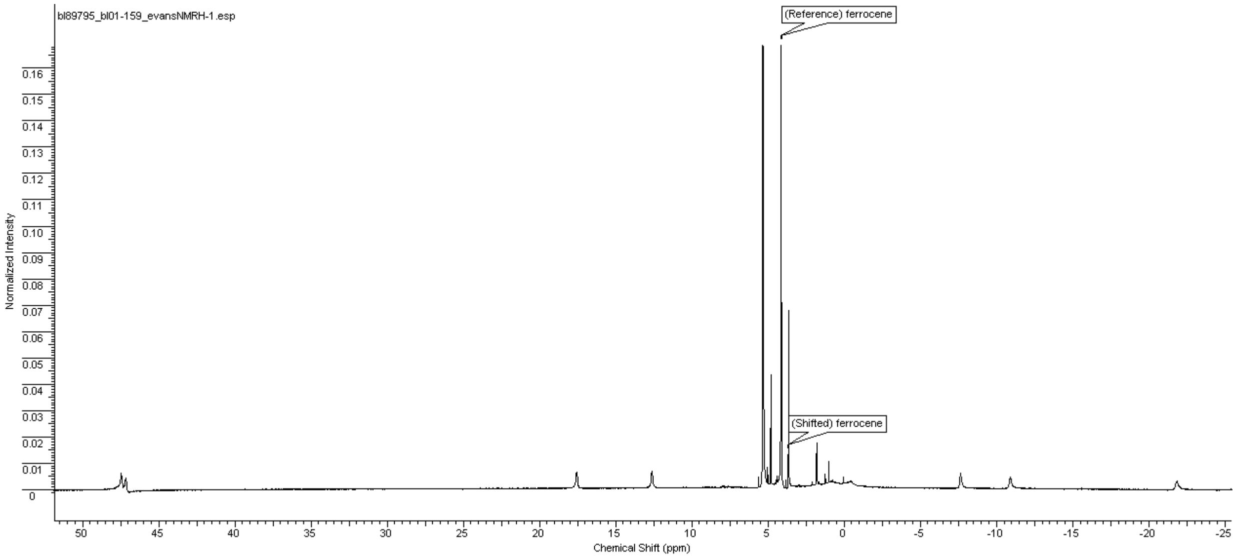
Preparation of [Iron ((±)-(*N*,*N*'-bis(pyridin-2-ylmethylene)cyclohexane-1,2-diamine) dichloride] [9FeCl$_2$]



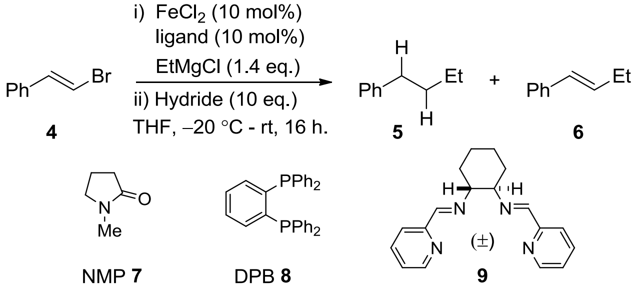
FeCl$_2$ (127 mg, 1 mmol) and ligand **9** (292 mg, 1 mmol) were dissolved in anhydrous THF (10 mL) and stirred for 4 hours at room temperature. The solvent was removed *in vacuo* and CH$_2$Cl$_2$ (20 mL) was added and the mixture stirred for 30 minutes. The mixture was filtered through a glass filter frit and the solvent removed *in vacuo* to give [Iron ((±)-(*N*,*N*'-bis(pyridin-2-ylmethylene)cyclohexane-1,2-diamine) dichloride] [**9**FeCl$_2$] (402 mg, 96%) as a dark blue solid. δ_H (300 MHz, CD$_2$Cl$_2$) 47.49 (app d, *J=90 Hz*), 17.66 (br s), 12.63 (br s), 3.67 (br s), 1.81 (br s), -7.75 (br s), -11.07 (br s), -22.07 (br s), -26.29 (br s).[2] ***μ*$_{eff}$** (Evans' method, CD$_2$Cl$_2$) = 5.14.[3]






bl89795_bl01-159_evansNMRH-1.esp
(Reference) ferrocene
(Shifted) ferrocene
Normalized Intensity
0.16
0.15
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
Chemical Shift (ppm)

Experimental for Table 1 - Reaction optimisation



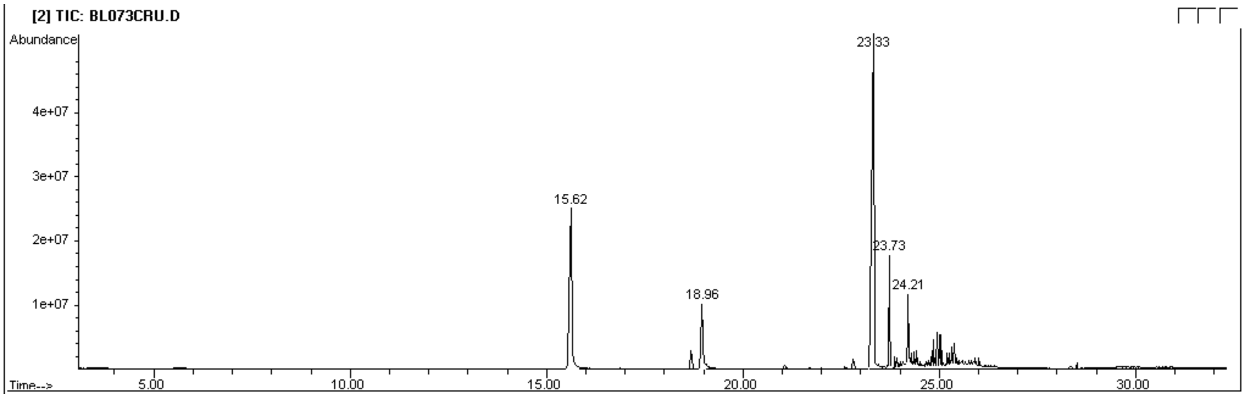
			Conversion (%)[b]	
Entry	Hydride	Ligand	Alkane XXX	Alkene XXX
1	$NaHBEt_3$	NMP **7**	9	53
2	$NaHBEt_3$	DPB **8**	2	91
3	$NaHBEt_3$	**9**	56	44
4	$NaHB(OAc)_3$	**9**	-	78
5	$LiHAl(O^tBu)_3$	**9**	25	73
6	KHB^sBu_3	**9**	55	44
7	$LiHBEt_3$	**9**	73	27
8	LiH_3BNMe_2	**9**	99	-
9	LiH_3BNMe_2	-	61	24
10	$NaBH_4$	**9**	-	93
11	$LiAlH_4$	**9**	-	94
12	$HSiEt_3$	**9**	-	87

[a] Conditions: 1 mmol **4**, 10 mol% $FeCl_2$, 10 mol% ligand, THF (0.1 M), -20 °C, i) 1.4 eq. EtMgCl (2M in THF), 15 min, ii) 10 eq. hydride, warm to rt, 16 h. [b] Conversion measured by GC-MS of the crude reaction mixture by comparison to authentic samples. [c] 110 mol% NMP added.

Table 1 Optimisation of the iron-catalysed, hydride-mediated reductive cross-coupling[a]

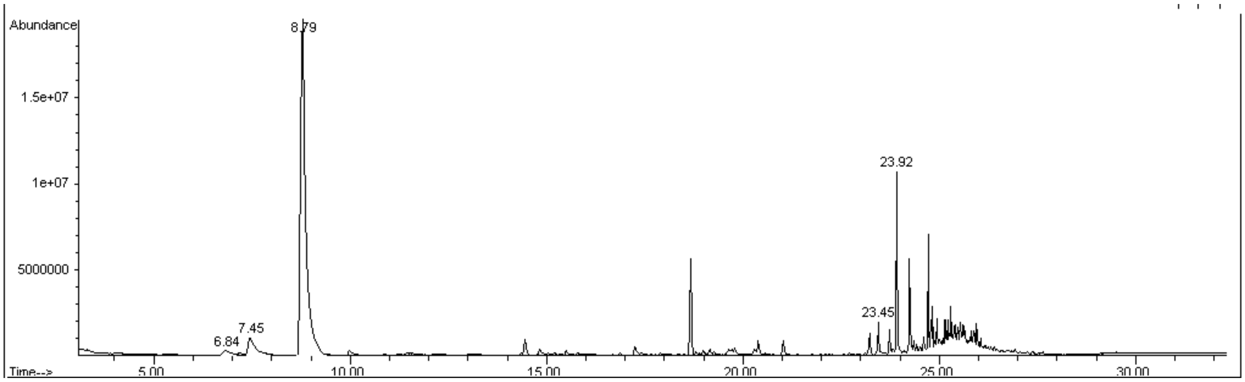
According to general procedure A; *β*-bromostyrene (0.13 mL, 1 mmol), $FeCl_2$ (13 mg, 0.1 mmol), ligand, organomagnesium chloride (0.7 mL, 2 M in THF) and sodium triethylborohydride (10 mL, 1 M in THF) were reacted in anhydrous THF (10 mL) to give the reduced cross-coupled products in varying quantities, determined by GC-MS [50-1] (Table 1).

$FeCl_2$ (10 mol%), NMP (110 mol%) (Table 1, Entry 1):



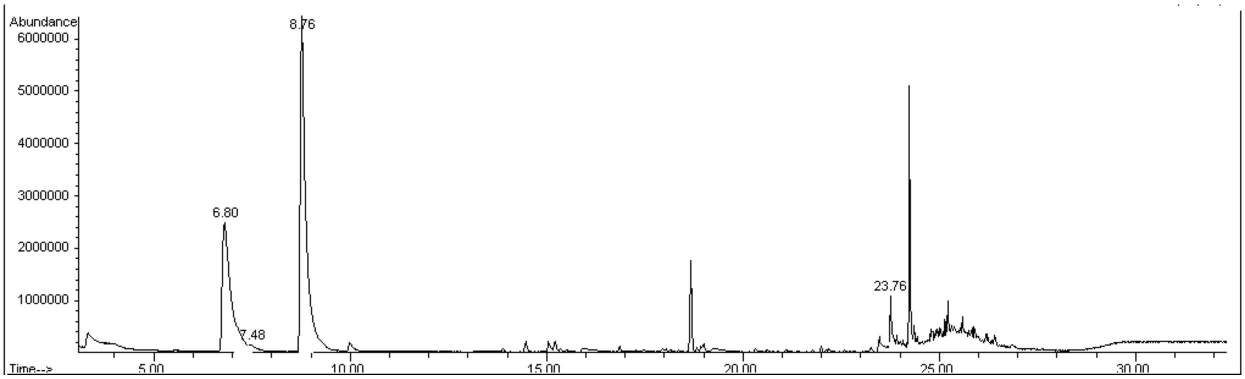
GC-MS [50-1]: biphenyl (15.6 min), bibenzyl (19.0 min), *trans*-stilbene (23.3 min), homo-coupled products (23.7-24.9 min).

$FeCl_2$ (10 mol%), 1,2-bis(diphenylphosphino)benzene (10 mol%) (Table 1, Entry 2):



GC-MS [50-1]: 1-phenyl-1-butene (7.45;8.79 min), homo-coupled product (23.7 min).

$FeCl_2$ (10 mol%), Ligand 9 (10 mol%) (Table 1, Entry 3):

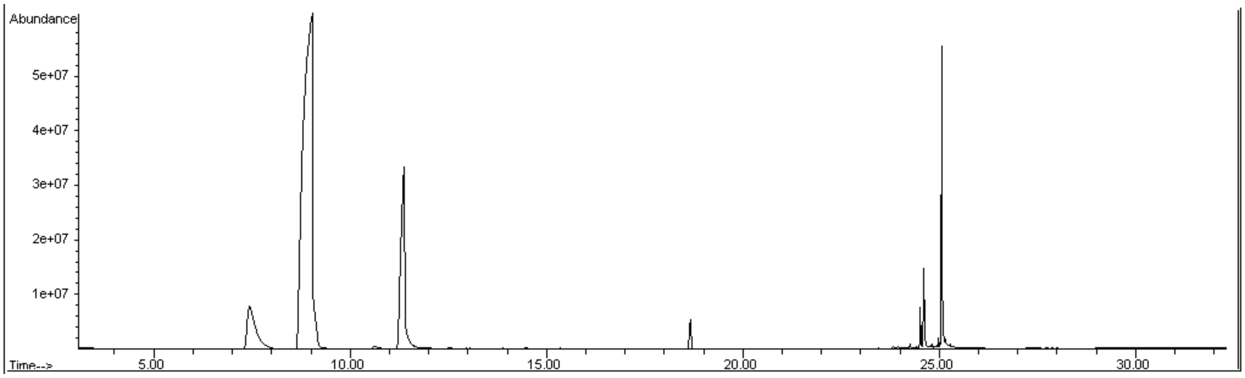


GC-MS [50-1]: butylbenzene (6.80 min), 1-phenyl-1-butene (7.48;8.76 min), homo-coupled product (23.8 min).

Reaction Optimisation (cont.) (Table 1)

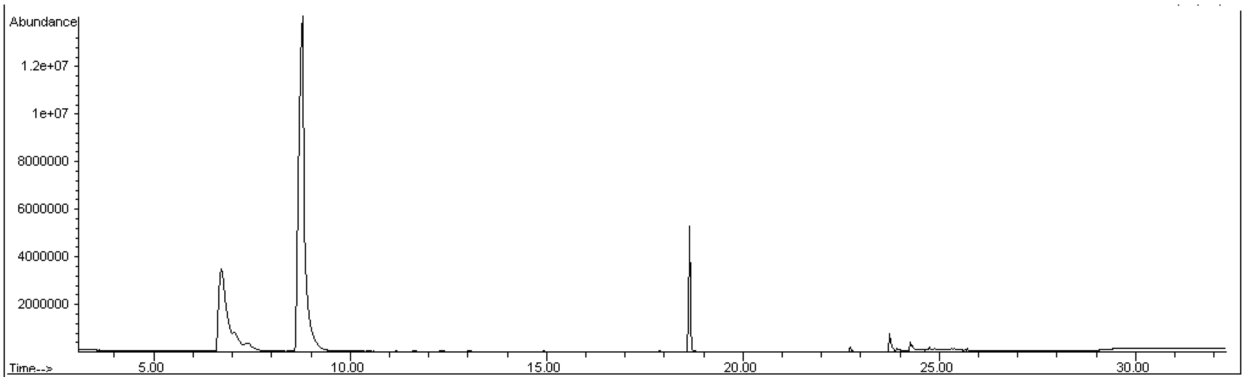
According to general procedure B; *β*-bromostyrene (0.13 mL, 1 mmol), iron catalyst [**9**$FeCl_2$] (13 mg, 0.1 mmol), ethylmagnesium chloride (0.7 mL, 2 M in THF) and hydride reagent were reacted in anhydrous THF (10 mL) to give the reduced cross-coupled products in varying quantities, determined by GC-MS [50-1] or [TE-labs] (Table 1).

[(9)$FeCl_2$] (10 mol%), $NaBH(OAc)_3$ (10 eq.) (Table 1, Entry 4):



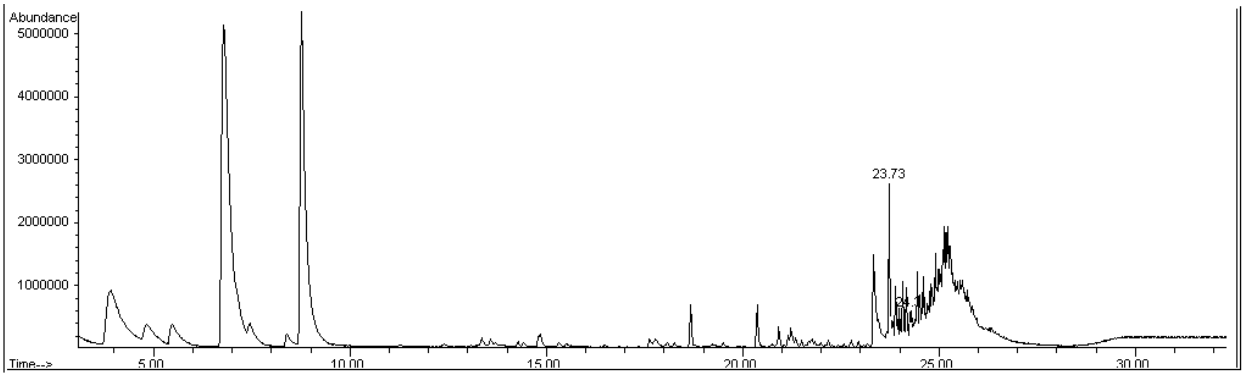
GC-MS [50-1]: 1-phenyl-1-butene (7.43;8.95 min), *β*-bromostyrene (11.3 min), homo-coupled products (24.5;24.6;25.1 min).

[(9)$FeCl_2$] (10 mol%), $LiAlH(O^tBu)_3$ (10 eq.) (Table 1, Entry 5):



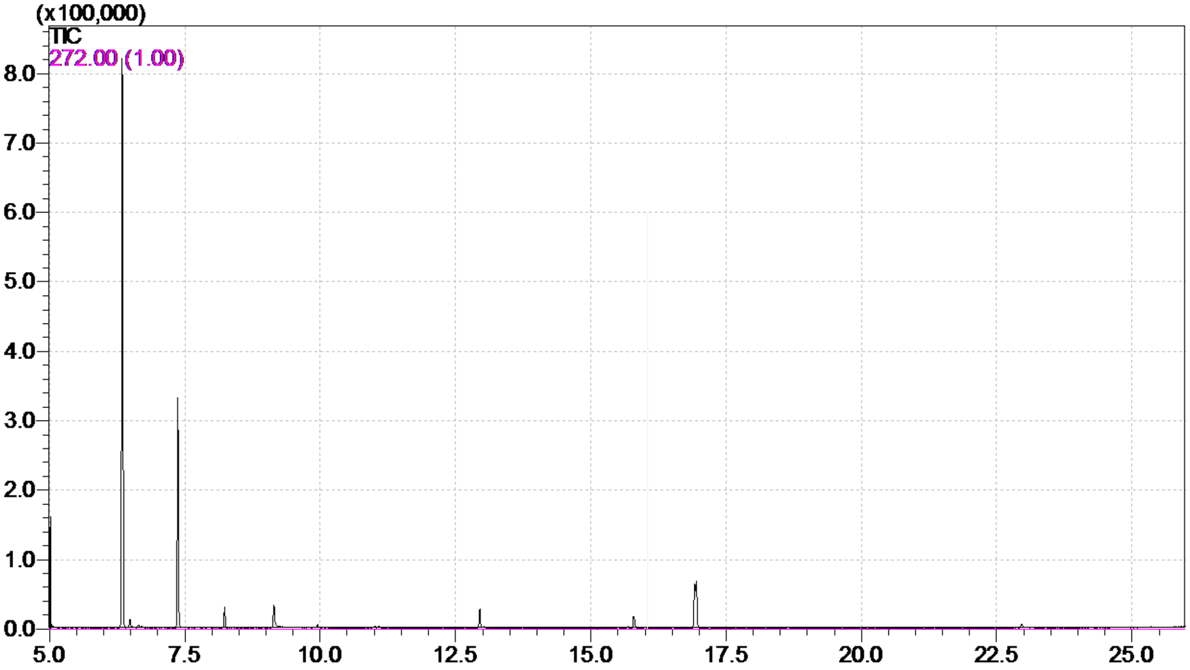
GC-MS [50-1]: butylbenzene (6.73 min), 1-phenyl-1-butene (7.39;8.77 min), homo-coupled products (23.8;24.3 min).

[(9)FeCl$_2$] (10 mol%), K-selectride (10 eq.) (Table 1, Entry 6):



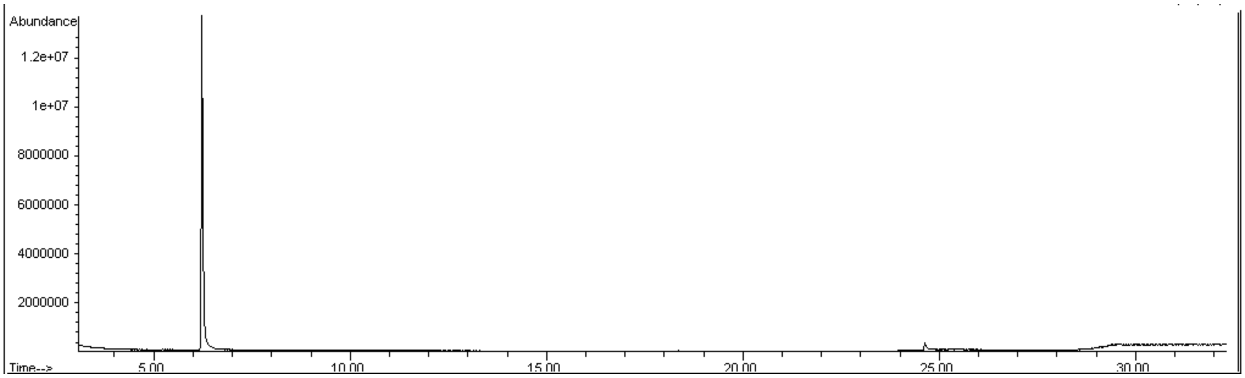
GC-MS [50-1]: butylbenzene (6.80 min), 1-phenyl-1-butene (7.47;8.79 min), homo-coupled products (23.7;24.3 min).

[(9)FeCl$_2$] (10 mol%), LiBH(Et)$_3$ (10 eq.) (Table 1, Entry 7):



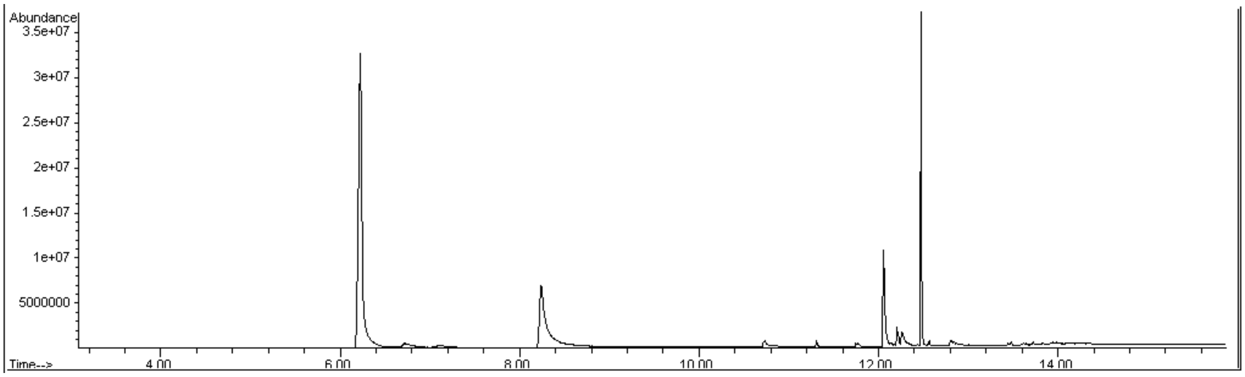
GC-MS [TE Labs]: butylbenzene (6.34 min), 1-phenyl-1-butene (6.48;7.37 min), homo-coupled product (22.9 min).

[(9)FeCl$_2$] (10 mol%), Me$_2$NBH$_3$Li (10 eq.) (Table 1, Entry 8):



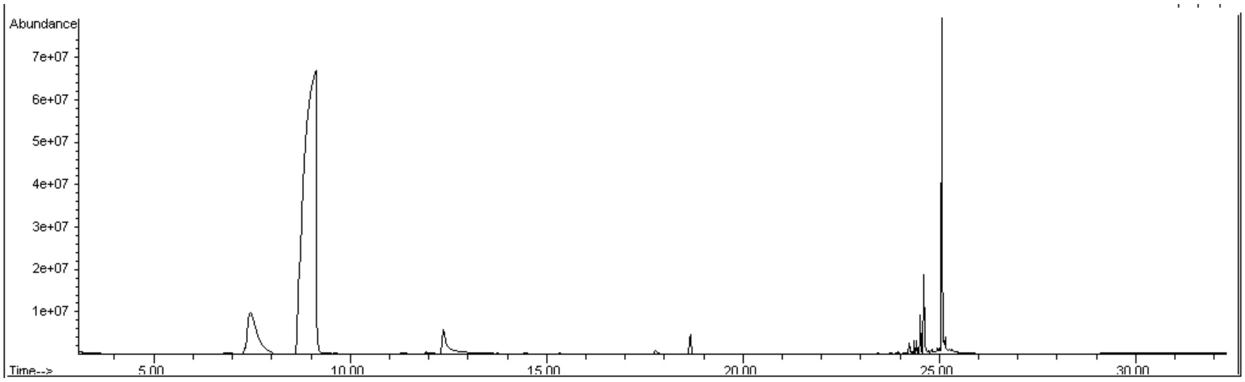
GC-MS [50-1]: butylbenzene (6.25 min).

FeCl$_2$ (10 mol%), Me$_2$NBH$_3$Li (10 eq.) (Table 1, Entry 9):



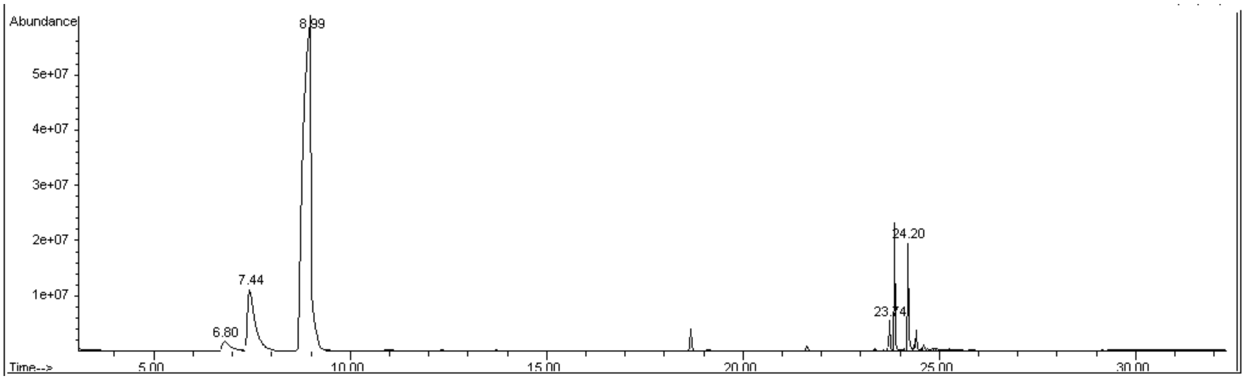
GC-MS [50-SPT]: butylbenzene (6.24 min), 1-phenyl-1-butene (6.74;8.23 min), homo-coupled products (12.05;12.26 min).

[(9)FeCl$_2$] (10 mol%), NaBH$_4$ (10 eq.) (Table 1, Entry 10):



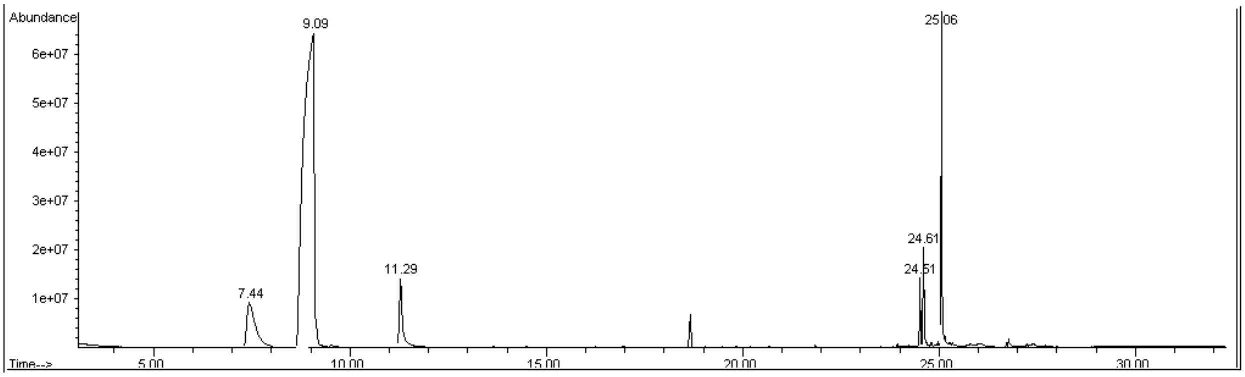
GC-MS [50-1]: butylbenzene (6.84 min), 1-phenyl-1-butene (7.43;9.05 min), homo-coupled products (24.5;24.6;25.1 min).

[(9)FeCl$_2$] (10 mol%), LiAlH$_4$ (10 eq.) (Table 1, Entry 11):



GC-MS [50-1]: butylbenzene (6.81 min), 1-phenyl-1-butene (7.44;8.94 min), homo-coupled products (23.7;24.2 min).

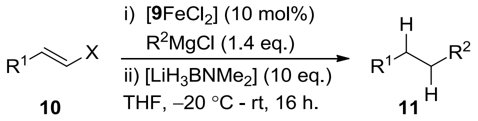
[(9)FeCl$_2$] (10 mol%), Et$_3$SiH (10 eq.) (Table 1, Entry 12):



GC-MS [50-1]: 1-phenyl-1-butene (7.43;8.92 min), *β*-bromostyrene (11.3 min), homo-coupled products (24.5;24.6;25.1 min).

Experimental for Table 2 - Substrate Scope

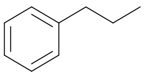
Table 2 Scope and limitation of the iron-catalysed, hydride-mediated reductive cross-coupling^{a}



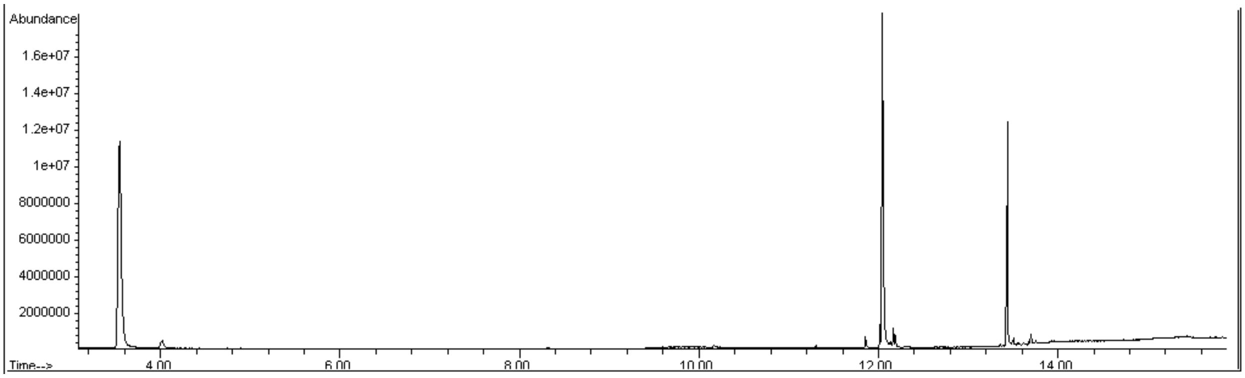
				Conversion (%)^{b}	
Entry	R^1	X	R^2	Alkane	**11**
1	Ph	Br	Me	53	**11a**
2	Ph	Br	Et	99 (84^{c})	**5**
3	Ph	Br	^{i}Pr	87	**11b**
4	Ph	Br	^{t}Bu	37^{d}	**11c**
5	Ph	Br	Ph	41^{e}	**11d**
6	Ph	Br	Allyl	35	**11e**^{f}
7	4-Me-Ph	I	Et	92 (87^{c})	**11f**
8	4-Me-Ph	Br	Et	91	**11f**
9	4-Me-Ph	Cl	Et	13^{g}	**11f**
10	4-Cl-Ph	Cl	Et	60	**5**
11	4-Cl-Ph	Br	Et	66	**5**
12	3,5-MeO-Ph	Br	Et	81	**11g**

Conditions: 1 mmol **10**, 10 mol% [**9**FeCl$_2$], THF (0.1 M), -20 °C, i) 1.4 eq. R^{2}MgCl (2M in THF), 15 min, ii) 10 eq. [LiH$_3$BNMe$_2$] (1.7 M in THF), warm to rt, 16 h. ^{b} Conversion measured by GC-MS of the crude reaction mixture by comparison to authentic samples. ^{c} Isolated yield. ^{d} 61% 1,4-diphenylbutane. ^{e} 40% biphenyl. . ^{f} Complete reduction of R^2 observed in the reaction, product **11e** R^2 = *n*-propyl. ^{g} 46% alkene.

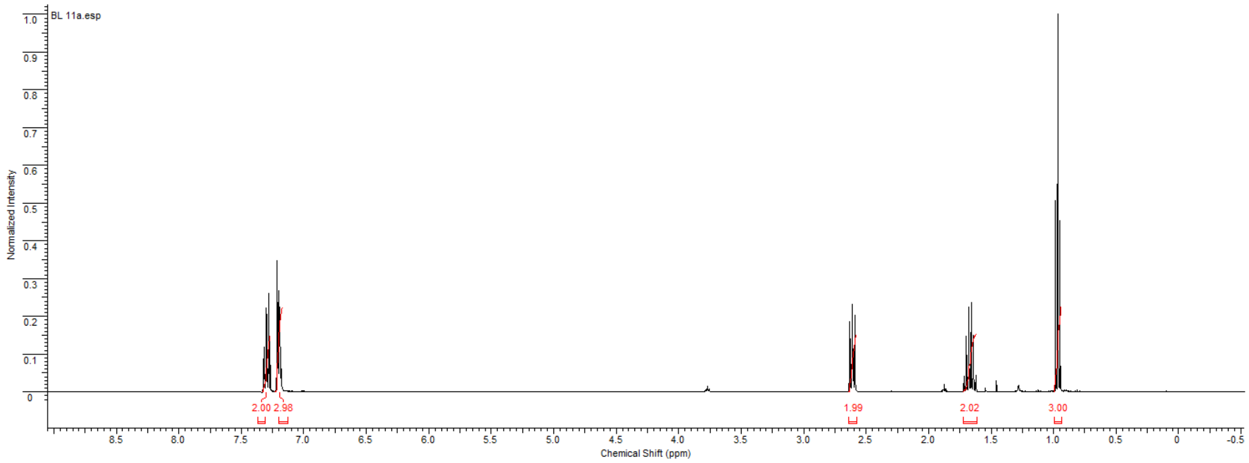
Propylbenzene 11a (Table 2, Entry 1)

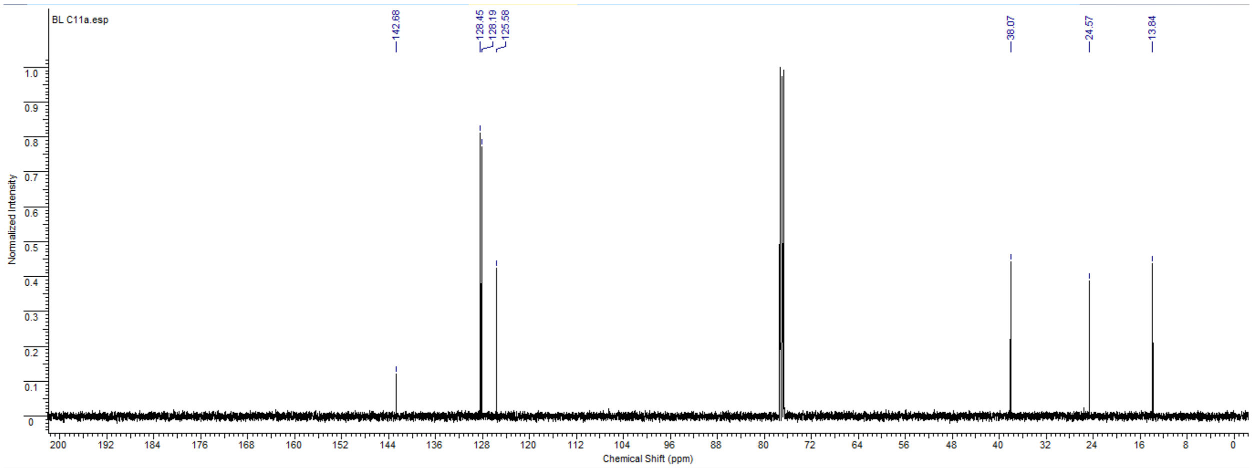


According to general procedure C; *β*-bromostyrene (0.13 mL, 1 mmol), iron catalyst [**9**FeCl$_2$] (42 mg, 0.1 mmol), methylmagnesium chloride (0.47 mL, 3M in THF) and lithium dimethylaminoborohydride (5.9 mL, 1.7 M in THF) were reacted in anhydrous THF (10 mL) to give propylbenzene (53%) and homo-coupled products (47%). GC-MS [50-SPT] (M$^+$, relative abundance): 3.55 min (120, 53%), 12.1 min (210 min, 30%), 13.4 min (208, 17%). δ_H (400 MHz, CDCl$_3$) 7.25-7.31 (2H, m), 7.17-7.20 (3H, m), 2.60 (2H, m), 1.66 (2H, m), 0.96 (3H, t, *J=7.4 Hz*). δ_C (100 MHz, CDCl$_3$) 142.7, 128.5, 128.2, 125.3, 38.1, 24.6, 13.8.[4]

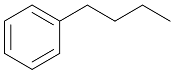


GC-MS [50-SPT]: propylbenzene (3.55 min), homo-coupled products (12.1;13.4 min).

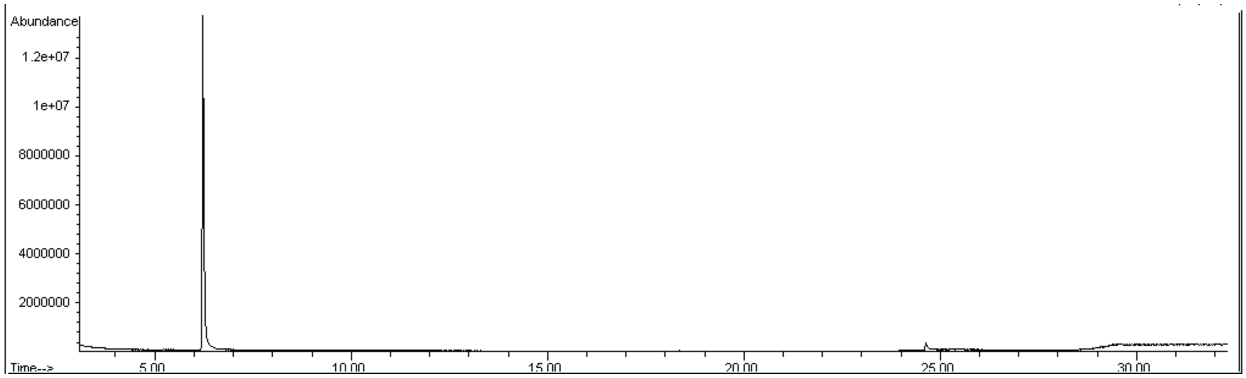




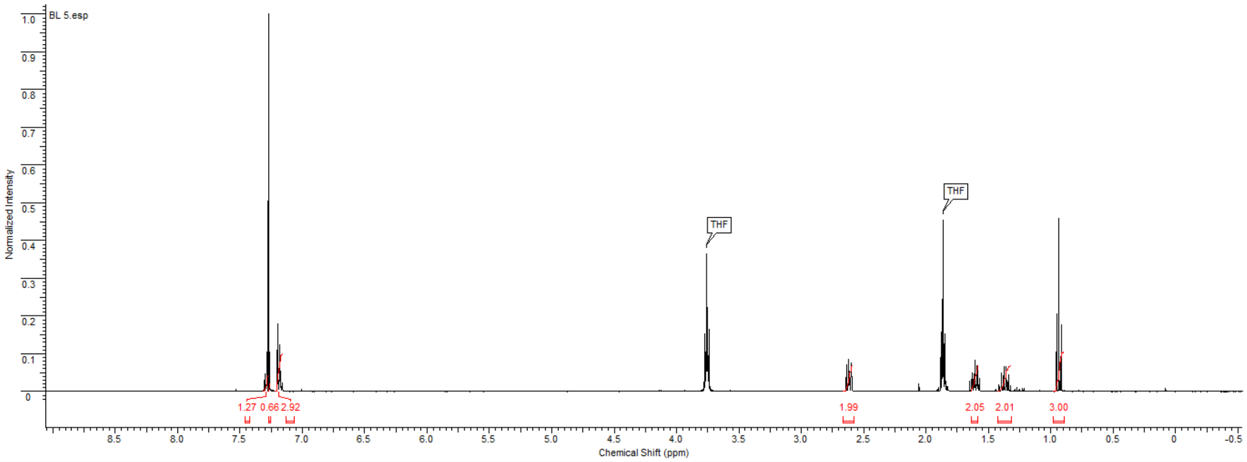
Butylbenzene 5 (Table 2, Entry 2)

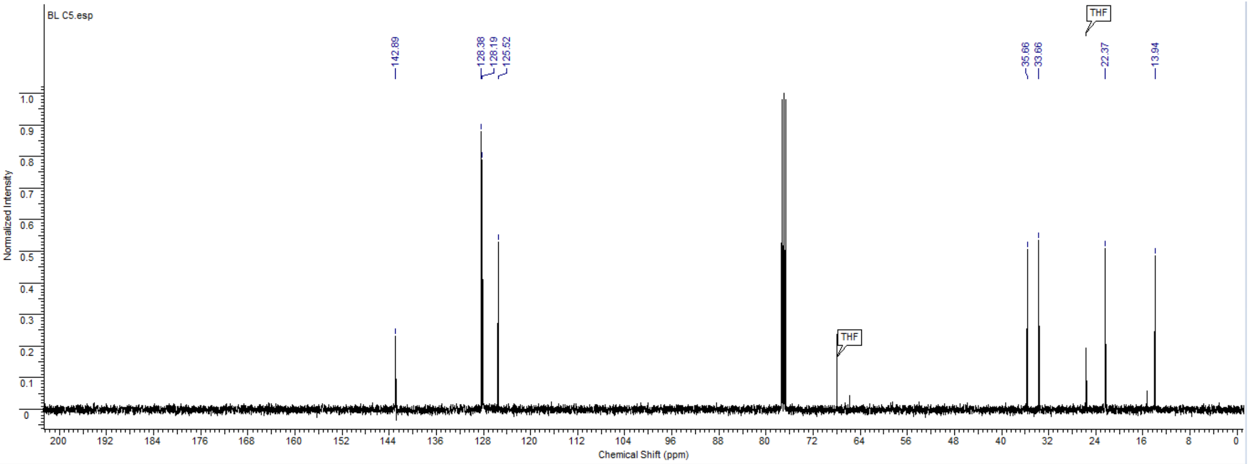


According to general procedure C; *β*-bromostyrene (0.13 mL, 1 mmol), iron catalyst [**9**$FeCl_2$] (42 mg, 0.1 mmol), ethylmagnesium chloride (0.7 mL, 2 M in THF) and lithium dimethylaminoborohydride (5.9 mL, 1.7 M in THF) were reacted in anhydrous THF (10 mL) to give butylbenzene (>99%). GC-MS [50-1] (M^+, relative abundance): 6.25 min (134, >99%). The product was isolated by flash column chromatography (100% pentane) to give butylbenzene (84%). δ_H (400 MHz, $CDCl_3$) 7.31-7.26 (2H, m), 7.21-7.15 (3H, m), 2.62 (2H, t, *J=7.7 Hz*), 1.61 (2H, m), 1.37 (2H, m), 0.94 (3H, t, *J=7.3 Hz*). δ_C (100 MHz, $CDCl_3$) 142.9, 128.4, 128.2, 125.5, 35.7, 33.7, 22.4, 13.9.[5]

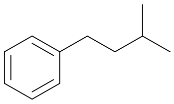


GC-MS [50-1]: butylbenzene (6.25 min).

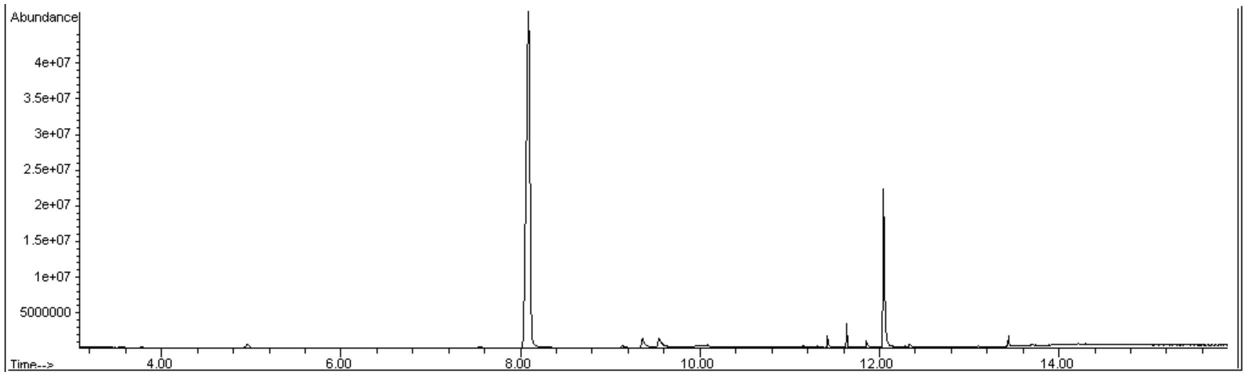




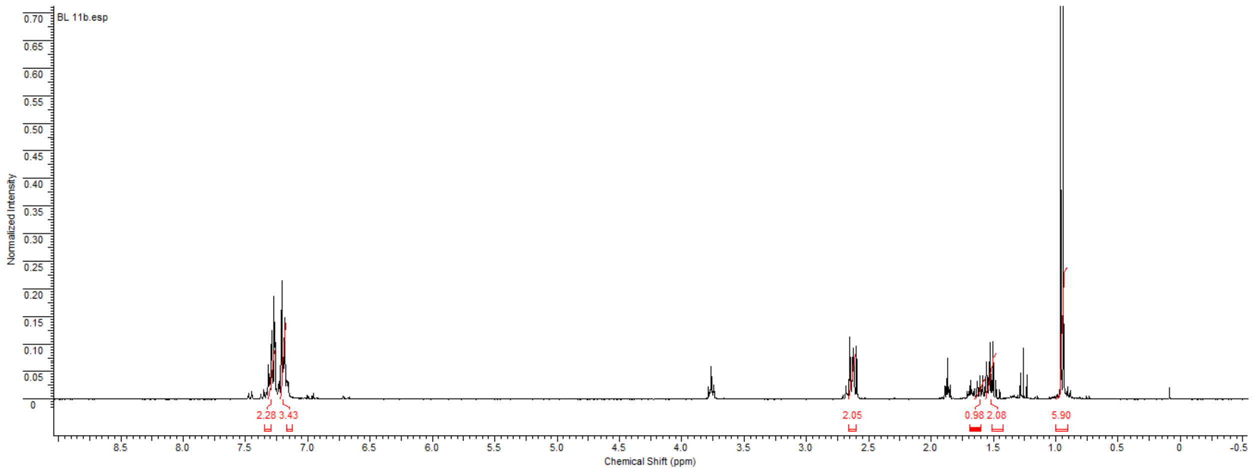
Isopentylbenzene 11b (Table 2, Entry 3)

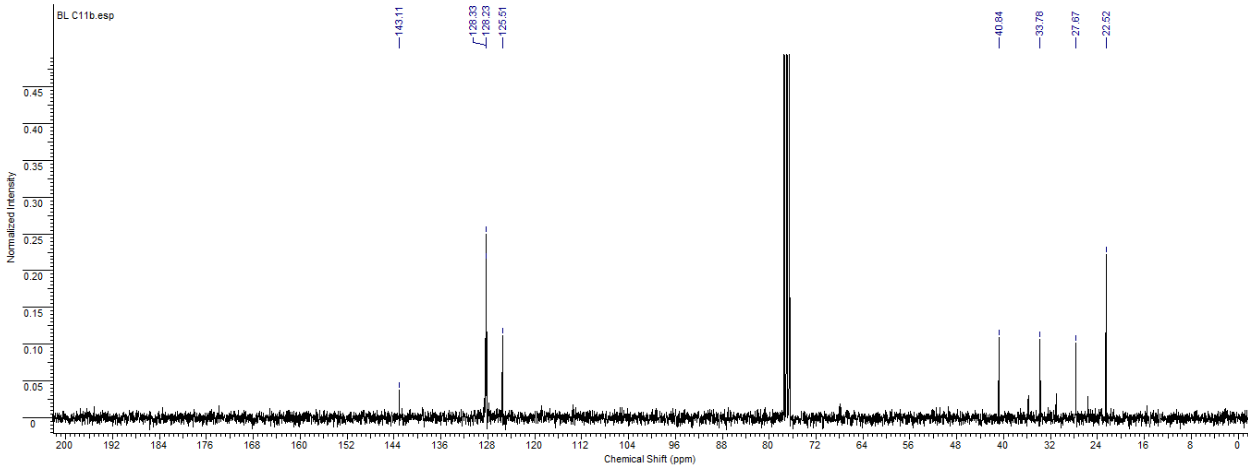


According to general procedure C; *β*-bromostyrene (0.13 mL, 1 mmol), iron catalyst [**9**$FeCl_2$] (42 mg, 0.1 mmol), isopropylmagnesium chloride (0.7 mL, 2 M in THF) and lithium dimethylaminoborohydride (5.9 mL, 1.7 M in THF) were reacted in anhydrous THF (10 mL) to give isopentylbenzene (87%) and a homo-coupled product (13%). GC-MS [50-SPT] (M^+, relative abundance): 8.09 min (148, 87%), 12.1 min (210, 13%). δ_H (400 MHz, $CDCl_3$) 7.32-7.26 (2H, m), 7.21-7.15 (3H, m), 2.62 (2H, m) 1.60 (1H, m), 1.52 (2H, m), 0.95 (6H, d, *J= 6.6 Hz*). δ_C (100 MHz, $CDCl_3$) 143.1, 128.3, 128.2, 125.5, 40.8, 33.8, 27.7, 22.5.[6]

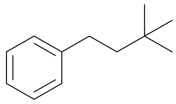


GC-MS [50-SPT]: isopentylbenzene (8.09 min), homo-coupled product (12.1 min).

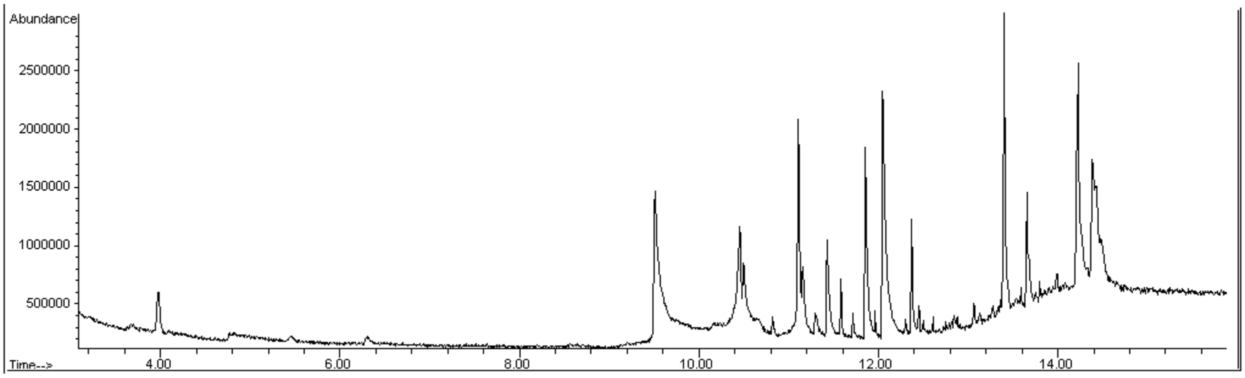




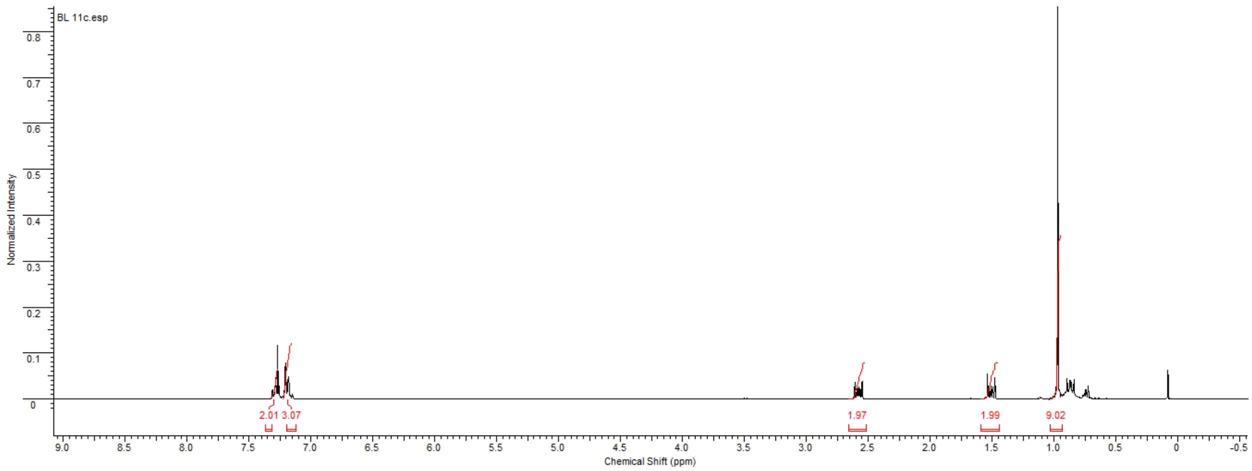
(3,3-dimethyl)butylbenzene 11c (Table 2, Entry 4)

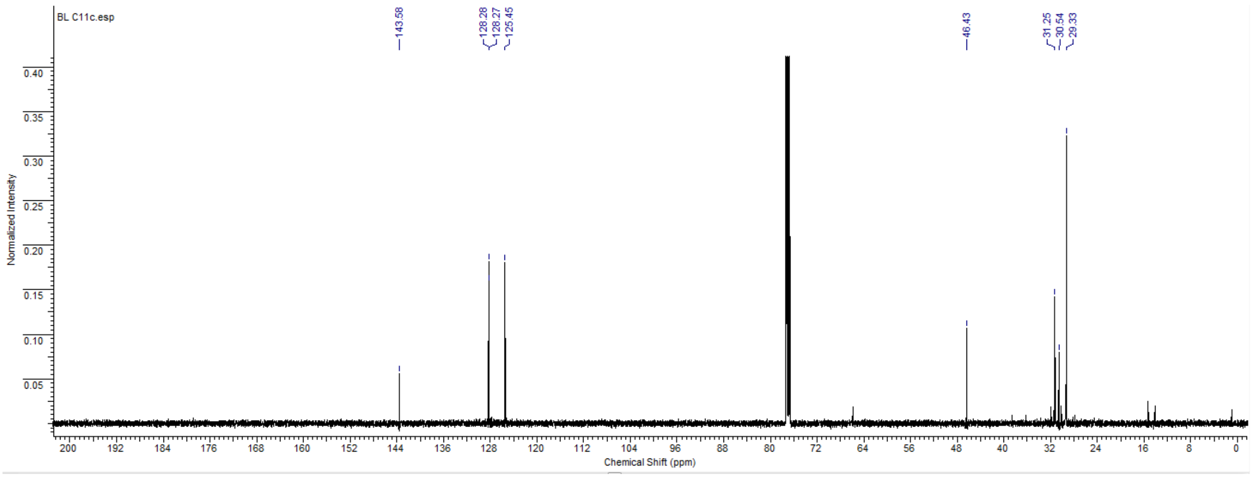


According to general procedure C; *β*-bromostyrene (0.13 mL, 1 mmol), iron catalyst [**9**$FeCl_2$] (42 mg, 0.1 mmol), *tert*-butylmagnesium chloride (1.4 mL, 1 M in THF) and lithium dimethylaminoborohydride (5.9 mL, 1.7 M in THF) were reacted in anhydrous THF (10 mL) to give (3,3-dimethyl)butylbenzene (37%) and homo-coupled products (61%). GC-MS [50-SPT] (M^+, relative abundance): 9.53 min (162, 37%), 11.85;12.08 min (210, 37%), 13.4;13.7 min (208, 24%). δ_H (300 MHz, $CDCl_3$) 7.33-7.25 (2H, m), 7.23-7.14 (3H, m), 2.58 (2H, m), 1.51 (2H, m), 0.97 (9H, s). δ_H (126 MHz, $CDCl_3$) 143.6, 128.28, 128.27, 125.5, 46.4, 31.3, 30.5, 29.3.[7]

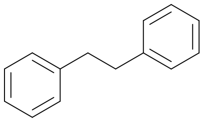


GC-MS [50-SPT]: (3,3-dimethyl)butylbenzene (9.53 min), homo-coupled products (11.85;12.1;13.4;13.7 min).

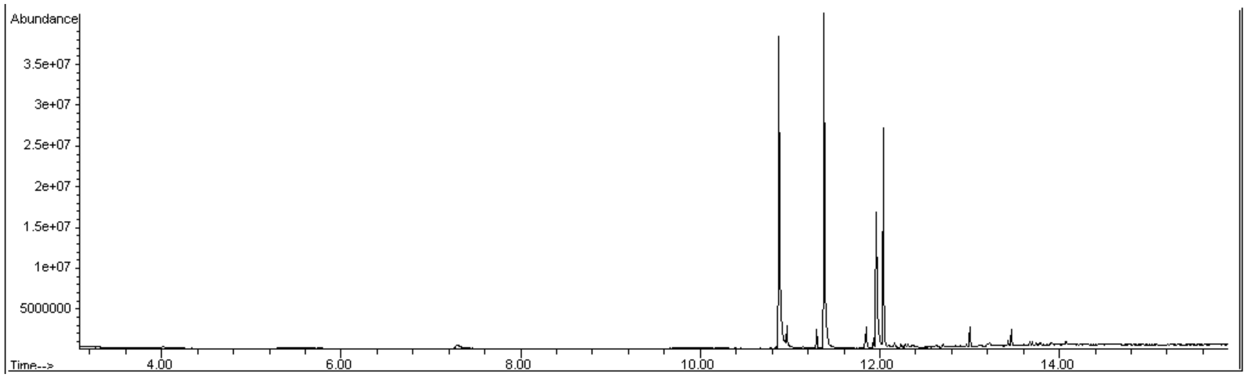




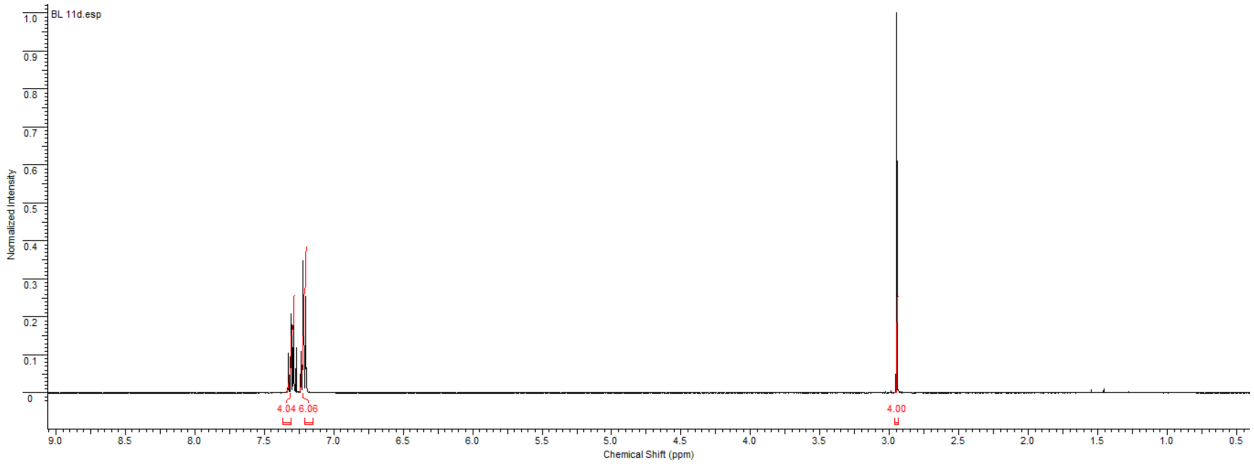
Bibenzyl 11d (Table 2, Entry 5)

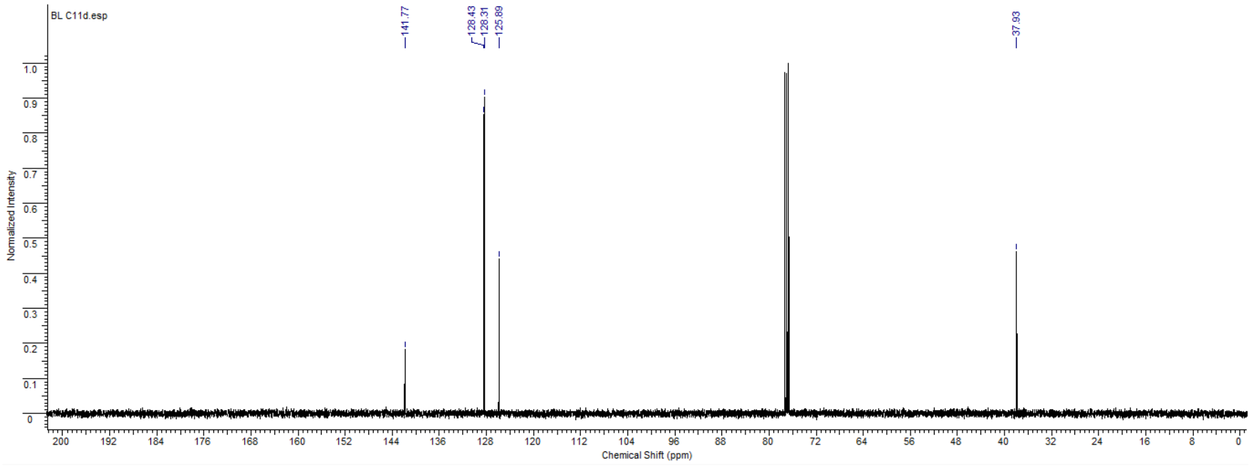


According to general procedure C; *β*-bromostyrene (0.13 mL, 1 mmol), iron catalyst [**9**$FeCl_2$] (42 mg, 0.1 mmol), phenylmagnesium chloride (0.7 mL, 2 M in THF) and lithium dimethylaminoborohydride (5.9 mL, 1.7 M in THF) were reacted in anhydrous THF (10 mL) to give bibenzyl (41%), biphenyl (40%) and homo-coupled products (19%). GC-MS [50-SPT] (M^+, relative abundance): 10.8 min (154, 40%), 11.4 min (182, 41%), 11.85;12.04 min (210, 19%). **Bibenzyl:** δ_H (400 MHz, $CDCl_3$) 7.34-7.28 (4H, m), 7.25-7.19 (6H, m), 2.95 (4H, s). δ_C (100 MHz, $CDCl_3$) 141.8, 128.4, 128.3, 125.9, 37.9.[8]

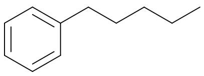


GC-MS [50-SPT]: biphenyl (10.8 min), bibenzyl (11.4 min) homo-coupled products (11.85;12.04 min).

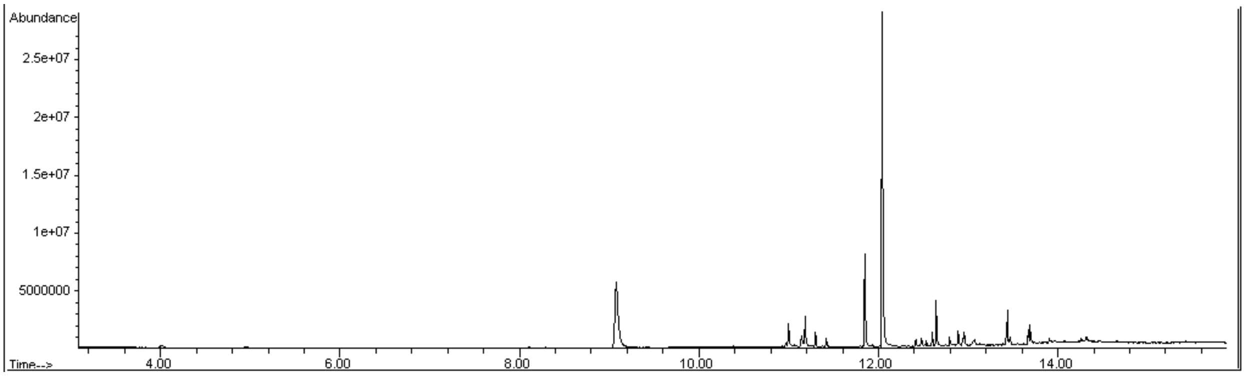




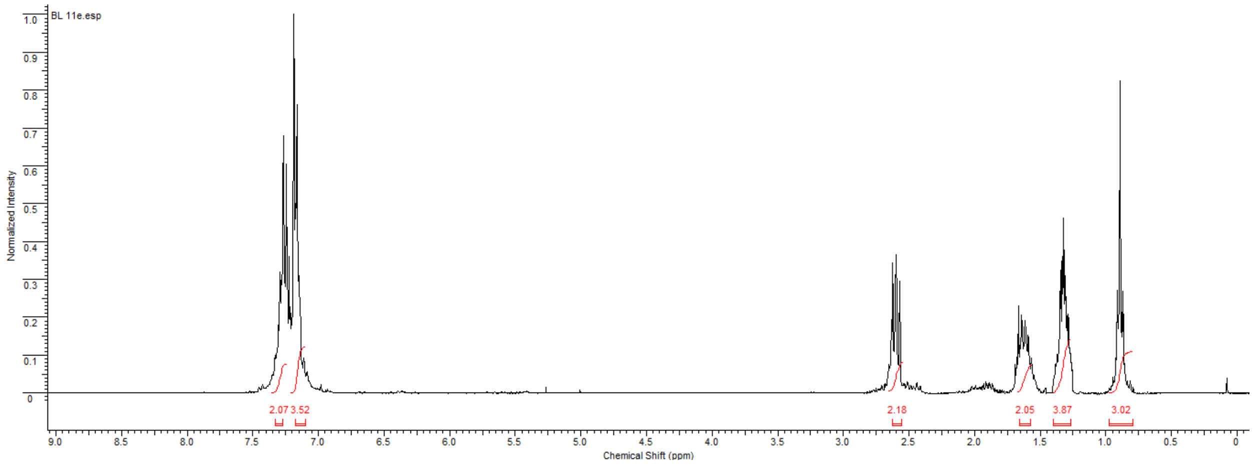
Pentylbenzene 11e (Table 2, Entry 6)

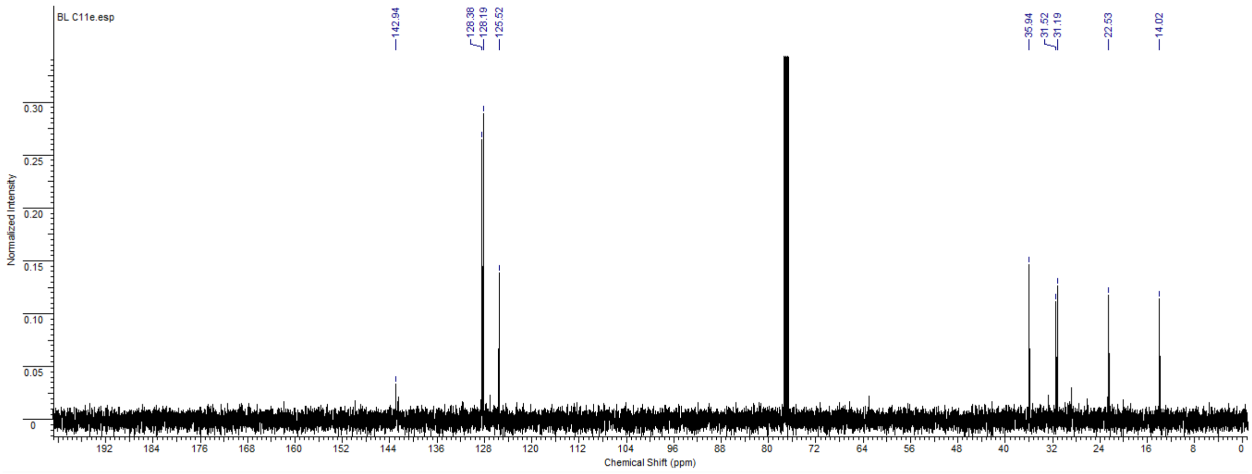


According to general procedure C; *β*-bromostyrene (0.13 mL, 1 mmol), iron catalyst [**9**$FeCl_2$] (42 mg, 0.1 mmol), allylmagnesium chloride (0.7 mL, 2 M in THF) and lithium dimethylaminoborohydride (5.9 mL, 1.7 M in THF) were reacted in anhydrous THF (10 mL) to give pentylbenzene (35%) and homo-coupled products (65%). GC-MS [50-SPT] (M^+, relative abundance): 9.09 min (148, 35%), 11.85;12.04 min (210, 56 %), 13.4 min (208, 9%). δ_H (400 MHz, $CDCl_3$) 7.30-7.24 (2H, m), 7.19-7.13 (2H, m), 2.63-2.56 (2H, m), 1.65-1.53 (2H, m), 1.37-1.25 (4H, m) 0.89 (3H, t, *J= 6.7 Hz*). δ_C (100 MHz, $CDCl_3$) 142.9, 128.4, 128.2, 125.5, 35.9, 31.5, 31.2, 22.5, 14.0. [10]

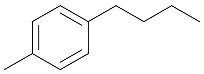


GC-MS [50-SPT]: pentylbenzene (9.09 min), homo-coupled products (11.85;12.04;13.4 min).

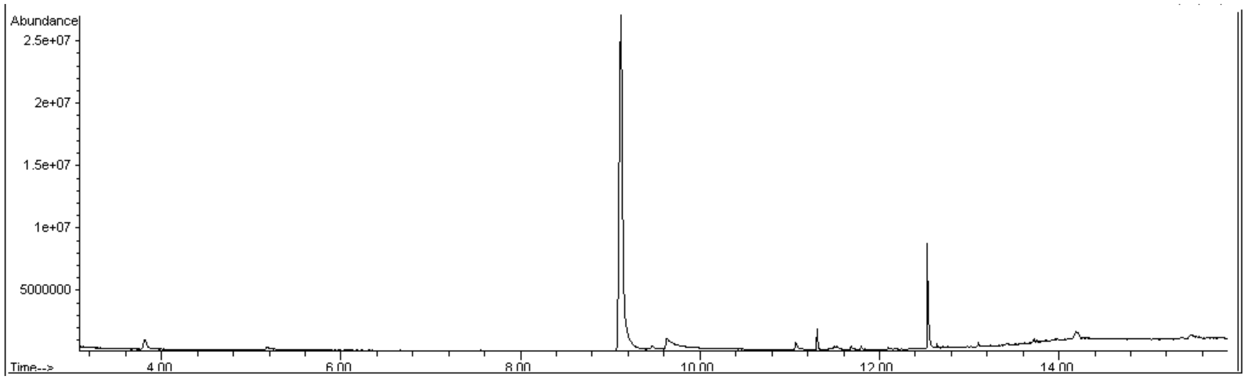




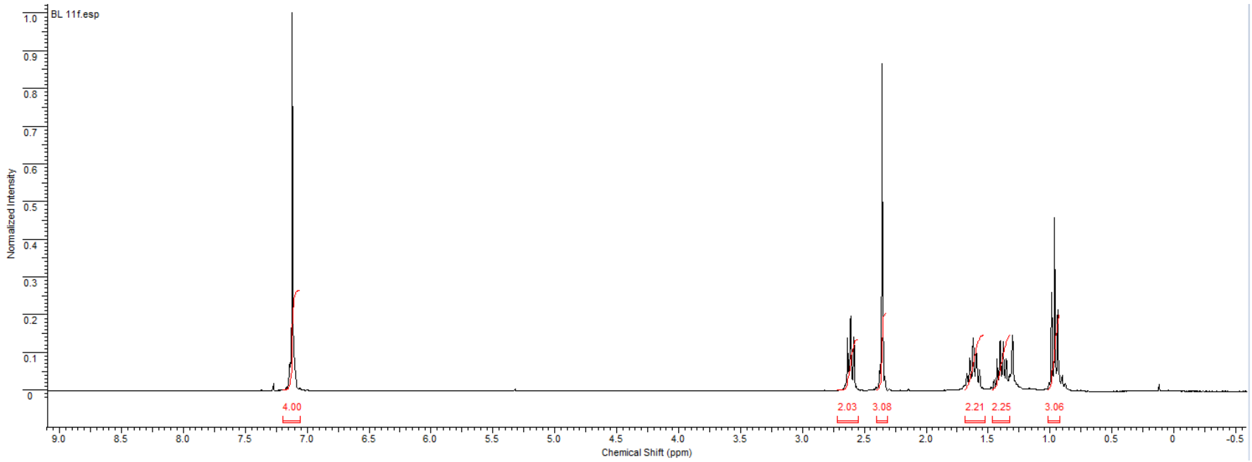
1-Butyl-4-methylbenzene 11f (from (*E*)-1-(2-iodovinyl)-4-methylbenzene and ethylmagnesium chloride) (Table 2, Entry 7)

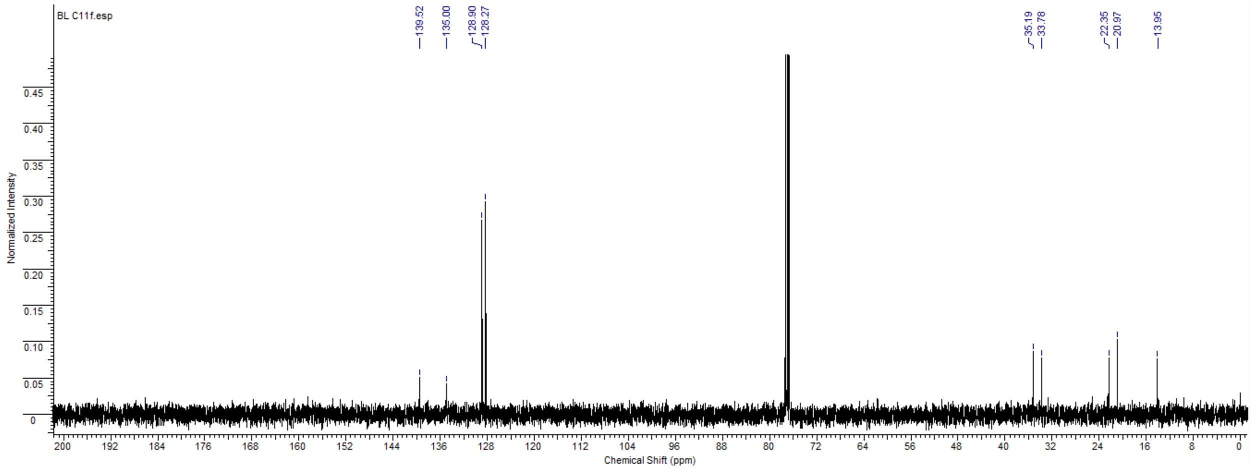


According to general procedure C; (*E*)-1-(2-iodovinyl)-4-methylbenzene (107 mg, 0.44 mmol), iron catalyst [**9**$FeCl_2$] (18 mg, 0.044 mmol), ethylmagnesium chloride (0.31 mL, 2 M in THF) and lithium dimethylaminoborohydride (2.6 mL, 1.7 M in THF) were reacted in anhydrous THF (5 mL) to give 1-butyl-4-methylbenzene (92%) and homo-coupled product (8%). GC-MS [50-SPT] (M^+, relative abundance): 9.13 min (148, 92%), 12.5 min (238, 8%). The product was isolated by flash column chromatography (100% pentane) to give 1-butyl-4-methylbenzene (87%). δ_H (300 MHz, $CDCl_3$) 7.08-7.17 (4H, m), 2.61 (2H, t, *7.7 Hz*), 2.36 (3H, s), 1.62 (2H, m), 1.39 (2H, m), 0.96 (3H, t, *J=7.3 Hz*). δ_C (100 MHz, $CDCl_3$) 139.5, 135.0, 128.9, 128.3, 35.2, 33.8, 22.4, 21.0, 14.0.[9,10]

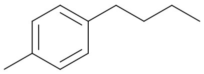


GC-MS [50-SPT]: 1-butyl-4-methylbenzene (9.13 min), homo-coupled product (12.5 min).

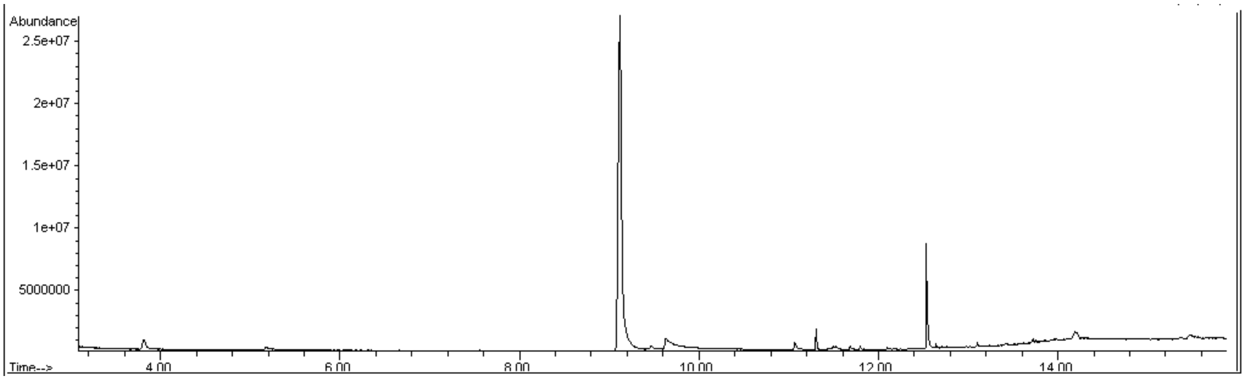




1-Butyl-4-methylbenzene 11f (from (*E*)-1-(2-iodovinyl)-4-methylbenzene and ethylmagnesium chloride) (Table 2, Entry 7)

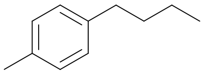


According to general procedure C; (*E*)-1-(2-bromovinyl)-4-methylbenzene (196 mg, 1 mmol), iron catalyst [**9**$FeCl_2$] (42 mg, 0.1 mmol), ethylmagnesium chloride (0.7 mL, 2 M in THF) and lithium dimethylaminoborohydride (5.9 mL, 1.7 M in THF) were reacted in anhydrous THF (10 mL) to give 1-butyl-4-methylbenzene (92%) and homo-coupled product (8%). GC-MS [50-SPT] (M^+, relative abundance): 9.15 min (148, 91%), 12.5 min (238, 9%). ^1H NMR data consistent with entry 7.[9,10]

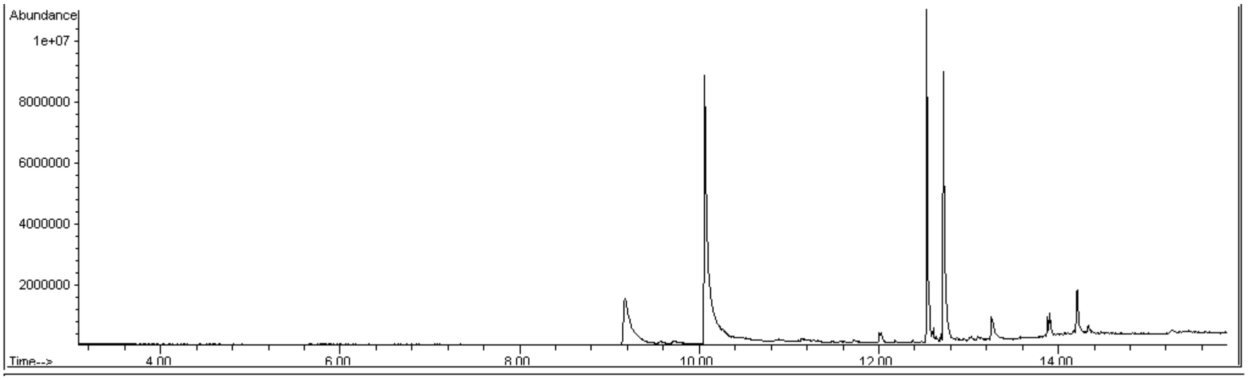


GC-MS [50-SPT]: 1-butyl-4-methylbenzene (9.15 min), homo-coupled product (12.5 min).

1-Butyl-4-methylbenzene 11f (from (*E*)-1-(2-chlorovinyl)-4-methylbenzene and ethylmagnesium chloride) (Table 2, Entry 9)

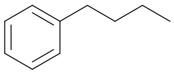


According to general procedure C; (*E*)-1-(2-chlorovinyl)-4-methylbenzene (153 mg, 1 mmol), iron catalyst [**9**$FeCl_2$] (42 mg, 0.1 mmol), ethylmagnesium chloride (0.7 mL, 2 M in THF) and lithium dimethylaminoborohydride (5.9 mL, 1.7 M in THF) were reacted in anhydrous THF (10 mL) to give 1-butyl-4-methylbenzene (13%), (*E*)-1-(4-methylphenyl)-1-butene (46%) and homo-coupled products (40%). GC-MS [50-SPT] (M^+, relative abundance): 9.17 min (148, 13%), 10.07 min (146, 46%), 12.02 min (152, 1%), 12.5 min (238, 20%), 12.7 min (236, 18%), 13.3 (234, 2%). ^1H NMR data consistent with entry 7.[9,10]

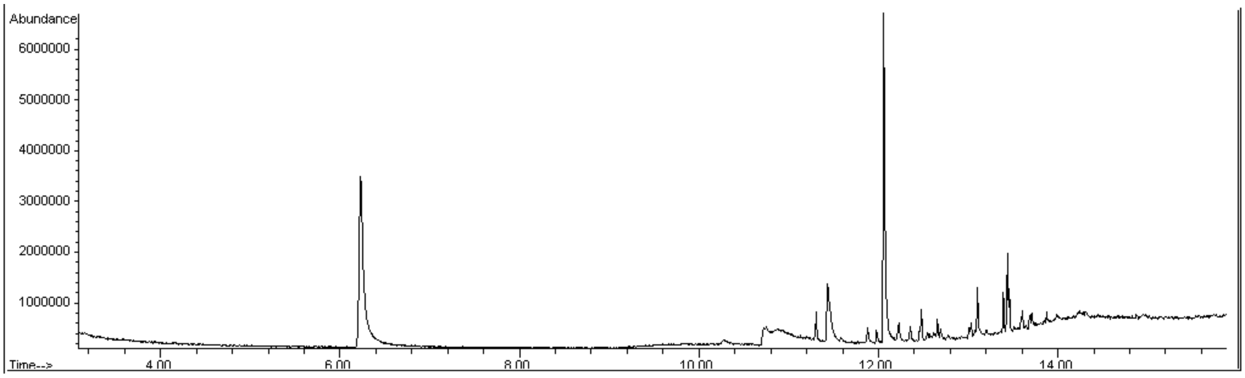


GC-MS [50-SPT]: 1-butyl-4-methylbenzene (9.17 min), (*E*)-1-(4-methylphenyl)-1-butene (10.07 min), (*E*)-1-(2-chlorovinyl)-4-methylbenzene (12.02 min), homo-coupled products (12.5;12,7;13.3 min).

Butylbenzene 5 (from (*E*)-1-(2-chlorovinyl)-4-chlorobenzene and ethylmagnesium chloride) (Table 2, Entry 10)

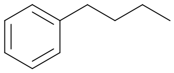


According to general procedure C; (*E*)-1-(2-chlorovinyl)-4-methylbenzene (83 mg, 0.48 mmol), iron catalyst [**9**$FeCl_2$] (20 mg, 0.048 mmol), ethylmagnesium chloride (0.34 mL, 2 M in THF) and lithium dimethylaminoborohydride (2.8 mL, 1.7 M in THF) were reacted in anhydrous THF (5 mL) to give butylbenzene (60%) and homo-coupled product (40%). GC-MS [50-SPT] (M^+, relative abundance): 6.24 min (134, 60%), 12.1 min (210, 40%). ^{1}H NMR consistent with entry 2.

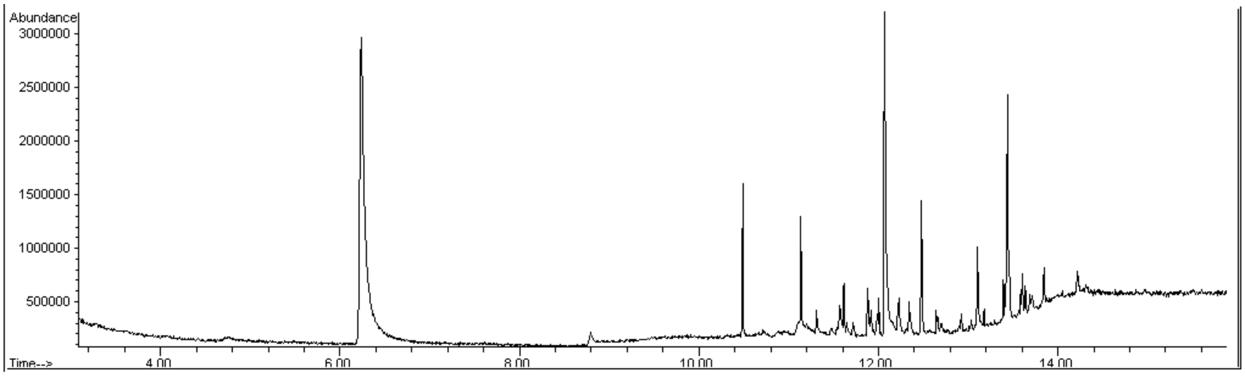


GC-MS [50-SPT]: butylbenzene (6.24 min), homo-coupled product (12.1 min)

Butylbenzene 5 (from (*E*)-1-(2-bromovinyl)-4-chlorobenzene and ethylmagnesium chloride) (Table 2, Entry 11)

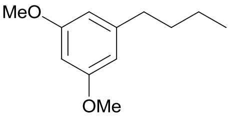


According to general procedure C; (*E*)-1-(2-bromovinyl)-4-methylbenzene (50 mg, 0.23 mmol), iron catalyst [**9**$FeCl_2$] (10 mg, 0.023 mmol), ethylmagnesium chloride (0.16 mL, 2 M in THF) and lithium dimethylaminoborohydride (1.35 mL, 1.7 M in THF) were reacted in anhydrous THF (3 mL) to give butylbenzene (66%) and homo-coupled products (34%). GC-MS [50-SPT] (M^+, relative abundance): 6.25 min (134, 66%), 12.1 min (210, 22%), 13.4 min (208, 12%). ^{1}H NMR consistent with entry 2.

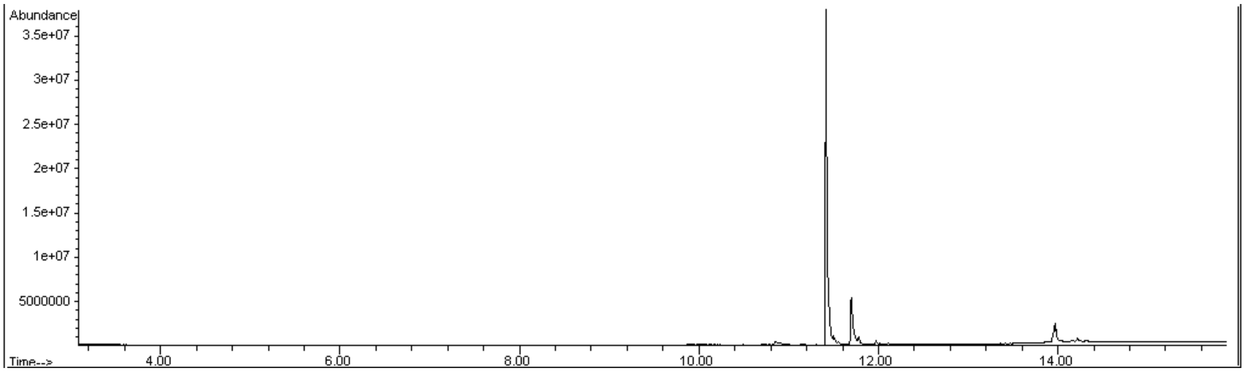


GC-MS [50-SPT]: butylbenzene (6.25 min), homo-coupled products (12.1;13.4 min).

1-Butyl-3,5-dimethoxybenzene 11g (from (*E*)-1-(2-bromovinyl)-3,5-dimethoxybenzene and ethylmagnesium chloride) (Table 2, Entry 12)

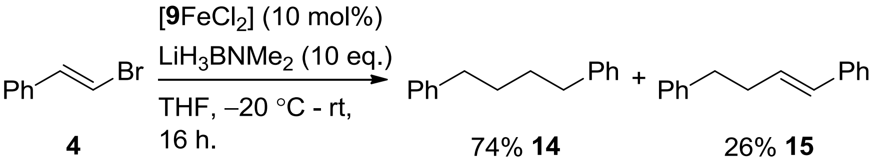


According to general procedure C; (*E*)-1-(2-bromovinyl)-3,5-dimethoxybenzene (118 mg, 0.485 mmol), iron catalyst **1** (20 mg, 0.0485 mmol), ethylmagnesium chloride (0.34 mL, 2 M in THF) and lithium dimethylaminoborohydride (2.85 mL, 1.7 M in THF) were reacted in anhydrous THF (5 mL) to give 1-butyl-3,5-dimethoxybenzene (81%), (*E*)-1-(but-1-en-1-yl)-3,5-dimethoxybenzene (18%) and homo-coupled products (>2%). GC-MS [50-SPT] (M^+, relative abundance): 11.4 min (194, 81%), 11.5;11.7 (192; 18%), 11.8 min (330, 1%), 13.0 min (328, <1%). δ_H (300 MHz, $CDCl_3$) 6.39-6.29 (3H, m), 3.77 (6H, s), 2.53 (2H, m), 1.58 (2H, m), 1.34 (2H, m), 0.91 (3H, t, *J=7.3 Hz*). δ_C (100 MHz, $CDCl_3$) 160.6, 145.3, 106.4, 97.4, 55.1, 35.9, 33.3, 22.3, 13.9.[11]



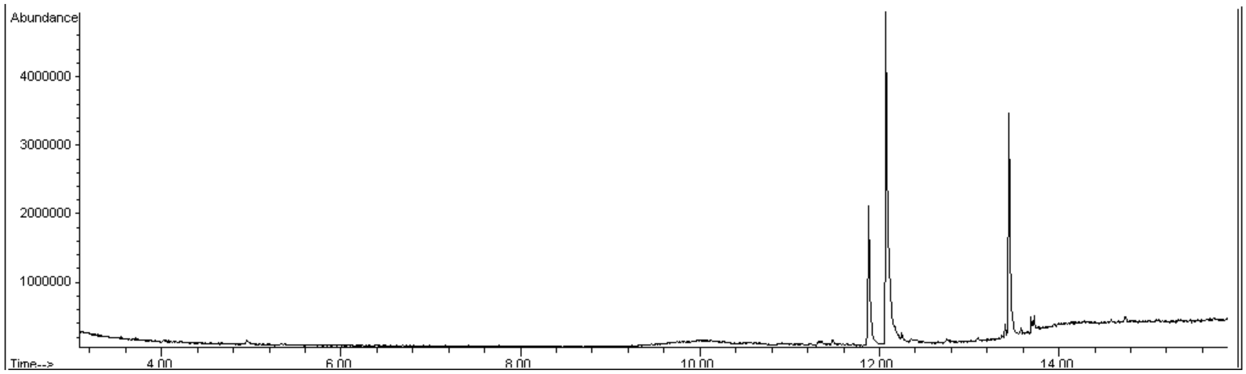
GC-MS [50-SPT]: 1-butyl-3,5-dimethoxybenzene (11.4 min), (*E*)-1-(but-1-en-1-yl)-3,5-dimethoxybenzene (11.5;11.7 min) homo-coupled products (11.8;13.0 min).

Reductive cross-coupling reaction in the absence of Grignard (Scheme 1)



Scheme 1 Iron-catalysed, hydride-mediated homo-coupling of β-bromostyrene

β-Bromostyrene (0.13 mL, 1 mmol) was added to a solution of iron catalyst [**9**$FeCl_2$] (42 mg, 0.1 mmol) in anhydrous THF (10 mL) and the mixture cooled to -20 °C. Lithium dimethylaminoborohydride (5.9 mL, 1.7 M in THF) was added dropwise and the reaction mixture was stirred for 16 h, allowing the bath and reaction mixture to warm to RT over this time. The solution was concentrated *in vacuo* and re-dissolved in CH_2Cl_2 (10 mL). Aqueous HCl (10 mL, 1 M) was added and the mixture stirred for 30 min. The aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL) and the combined organic extracts washed with H_2O (10 mL) and brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give 1,4-diphenylbutane (74%) and 1,4-diphenyl-1-butene (26%). GC-MS [50-SPT] (M^+, relative abundance): 11.9;12.1 min (210, 74%), 13.4 min (208, 26%).



GC-MS [50-SPT]: 1,4-diphenylbutane (11.9;12.1 min), 1,4-diphenyl-1-butene (13.4 min).

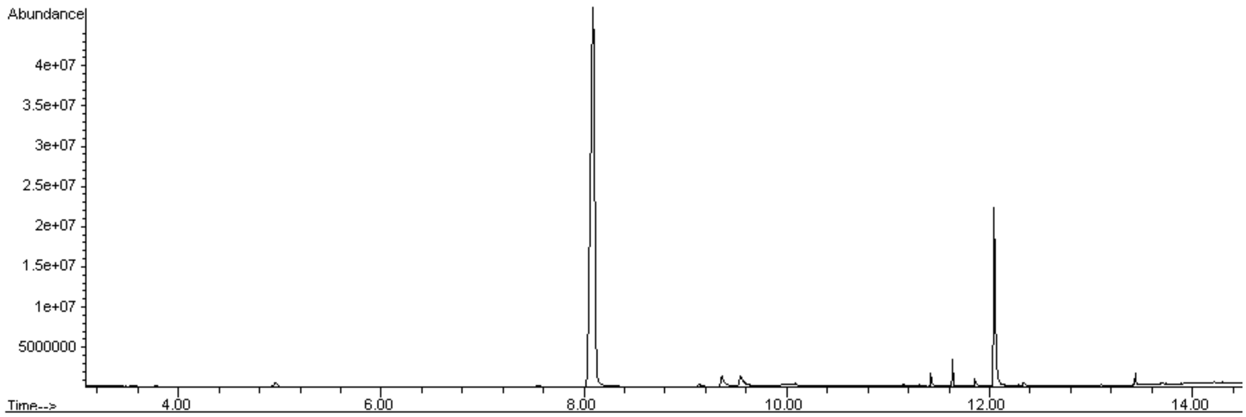
Investigation of potential catalytic role of trace metal impurities

Seven parallel reactions (A-G) were undertaken to investigate if trace metal impurities present in the iron salt used could have a role in the observed catalysis.[12] Copper(II) oxide, copper(II) chloride, nickel(II) acetylacetonate and cobalt(II) chloride were used.

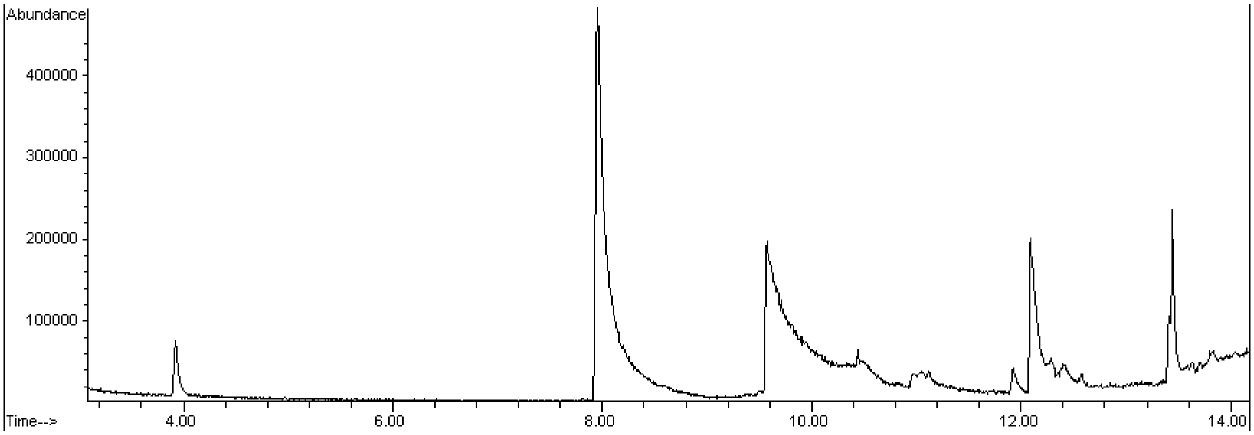
Reaction	**$FeCl_2$/mol%**	**Ligand 9/mol%**	**Metal Salt (1000ppm)**
A	10	10	-
B	10	10	Cu_2O
C	-	10	Cu_2O
D	10	10	$CuCl_2$
E	-	10	$CuCl_2$
F	10	10	$Ni(acac)_2$
G	-	10	$Ni(acac)_2$
H	10	10	$CoCl_2$
I	-	10	$CoCl_2$

β-bromostyrene (0.13 mL, 1 mmol) was added to a solution of catalyst system A-I in anhydrous THF and the mixture cooled to -20 °C. Isopropylmagnesium chloride (0.7 mL, 2 M in THF) was added dropwise and after 15 minutes lithium dimethylaminoborohydride (5.9 mL, 1.7 M in THF) was added dropwise. The reaction mixture was stirred for 16 hours, allowing the bath and reaction mixture to warm to room temperature over this time. The solution was concentrated *in vacuo* and re-dissolved in CH_2Cl_2. Aqueous HCl (10 mL, 1 M) was added and the mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL) and the combined organic extracts washed with H_2O (10 mL) and brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give the crude reaction products. Isopentylbenzene, isopentenylbenzene and a homo-coupled product, were detected by analysis by GC-MS [50-SPT].

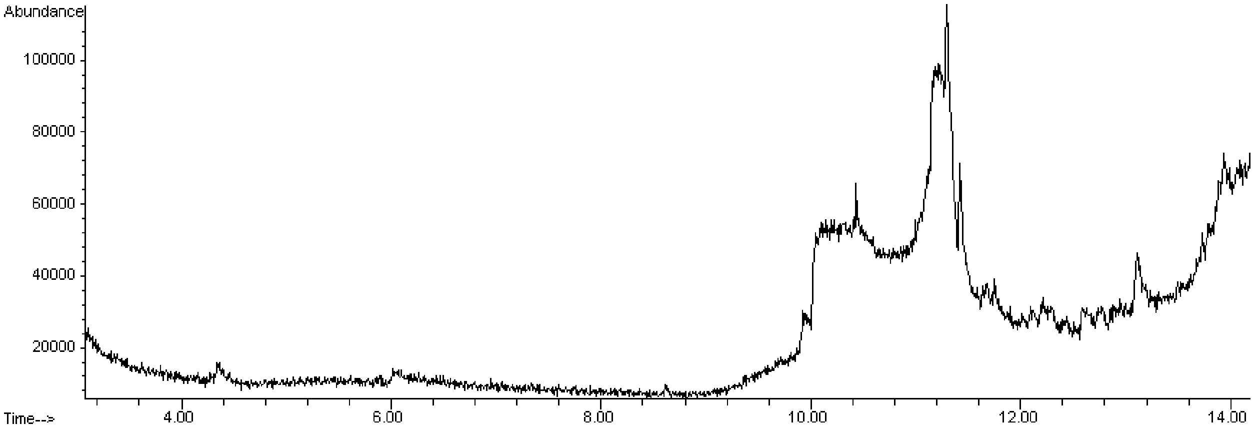
Reaction	**% Product (ret. Time, M^+)**		
	Isopentylbenzene (7.93, 148)	Isopentenylbenzene (9.52, 146)	Bibenzyl (12.05, 210)
A	80	7	13
B	52	37	11
C	-	trace	-
D	43	37	20
E	-	100	-
F	33	58	9
G	-	-	-
H	50	37	13
I	-	-	-



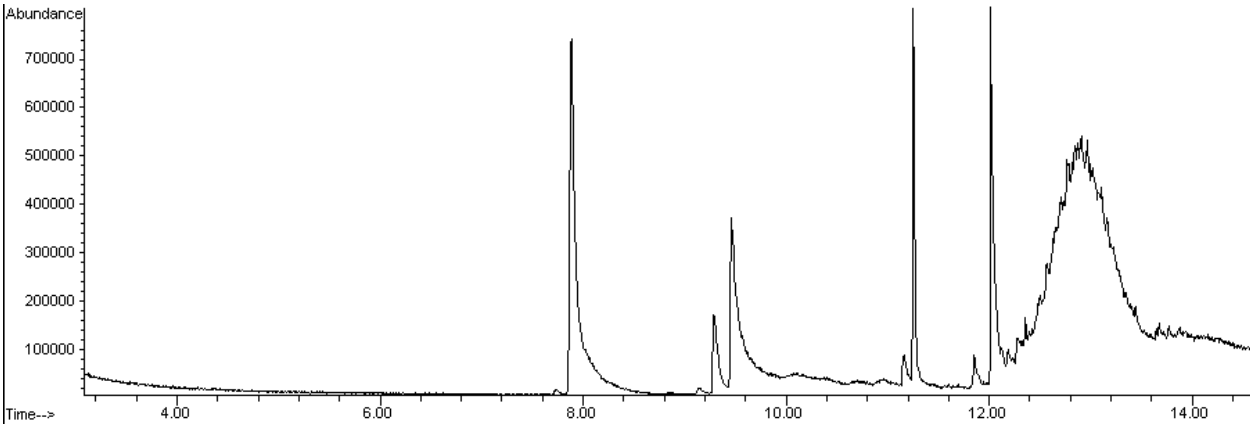
GC-MS [50-SPT]: Reaction A - 10mol% $FeCl_2$ + 10mol% Ligand **9**



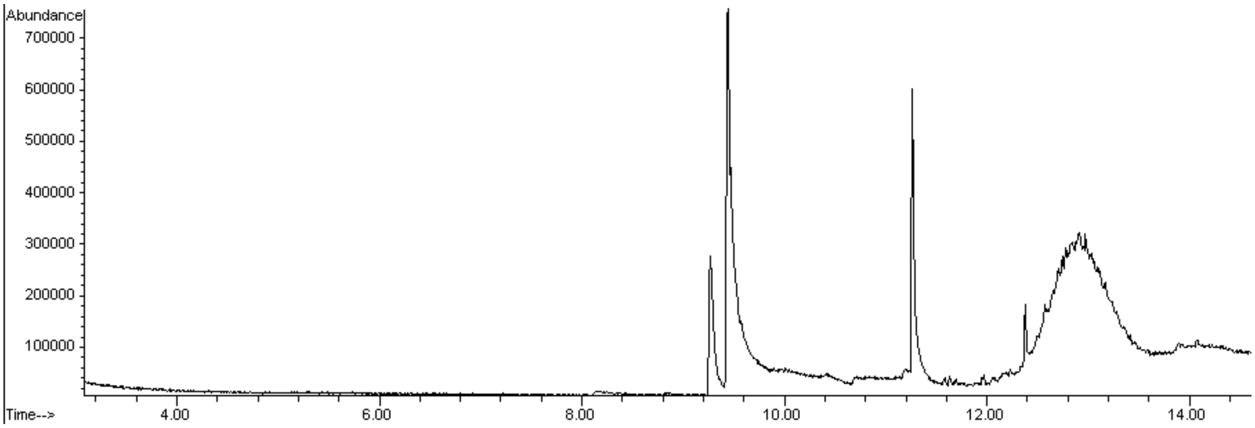
GC-MS [50-SPT]: Reaction B - 10mol% $FeCl_2$ + 10mol% Ligand **9** + 1000ppm Cu_2O



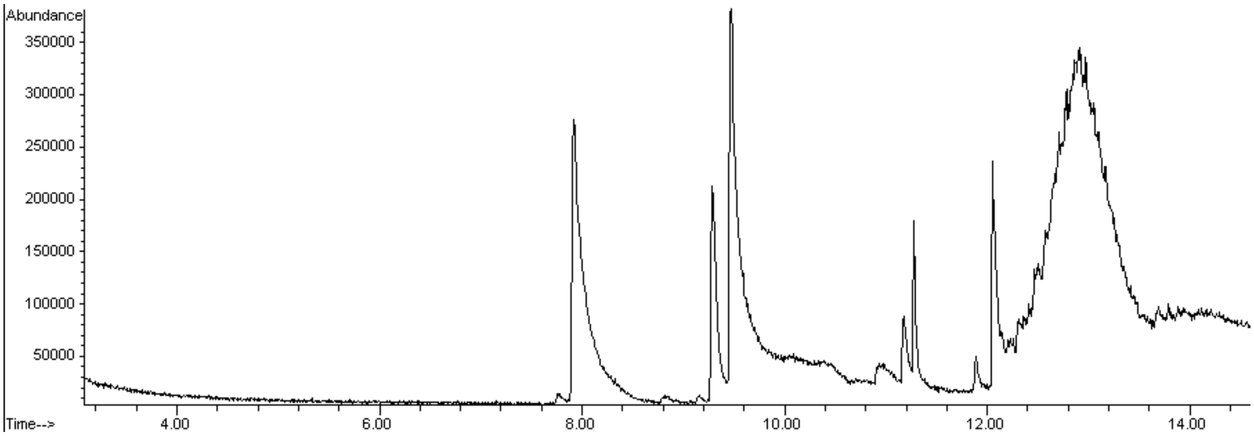
GC-MS [50-SPT]: Reaction C - no Fe + 10mol% Ligand **9** + 1000ppm Cu_2O



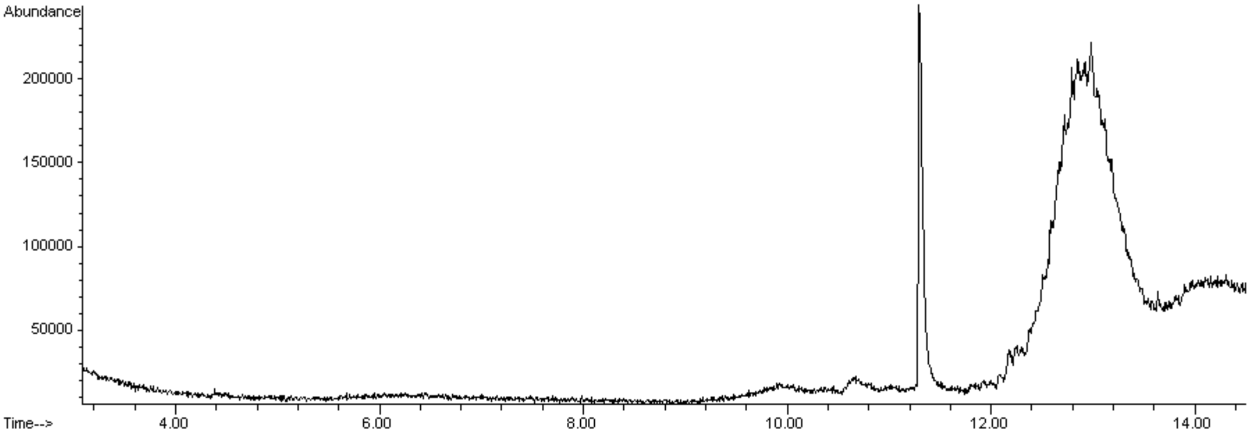
GC-MS [50-SPT]: Reaction D - 10mol% $FeCl_2$ + 10mol% Ligand **9** + 1000 ppm $CuCl_2$



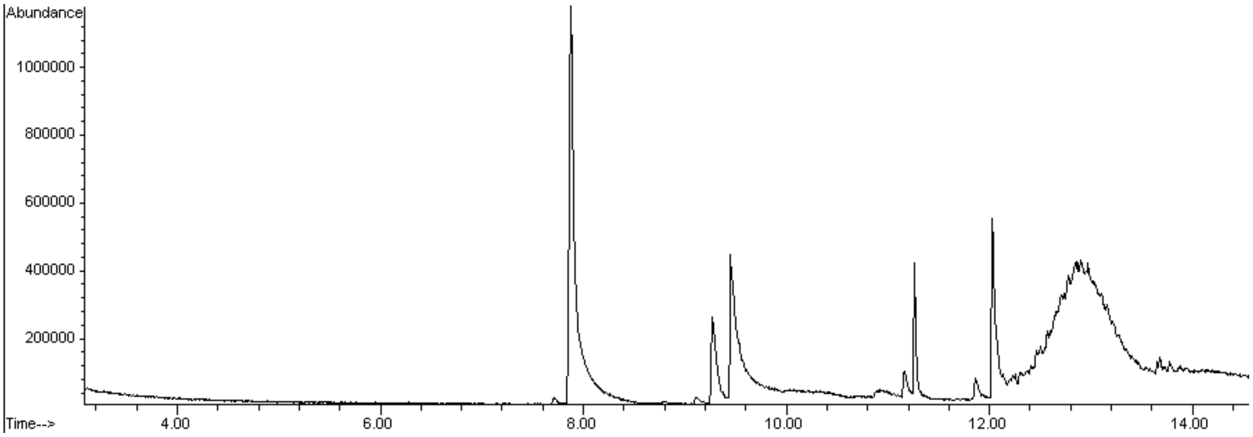
GC-MS [50-SPT]: Reaction E - no $FeCl_2$ + 10mol% Ligand **9** + 1000 ppm $CuCl_2$



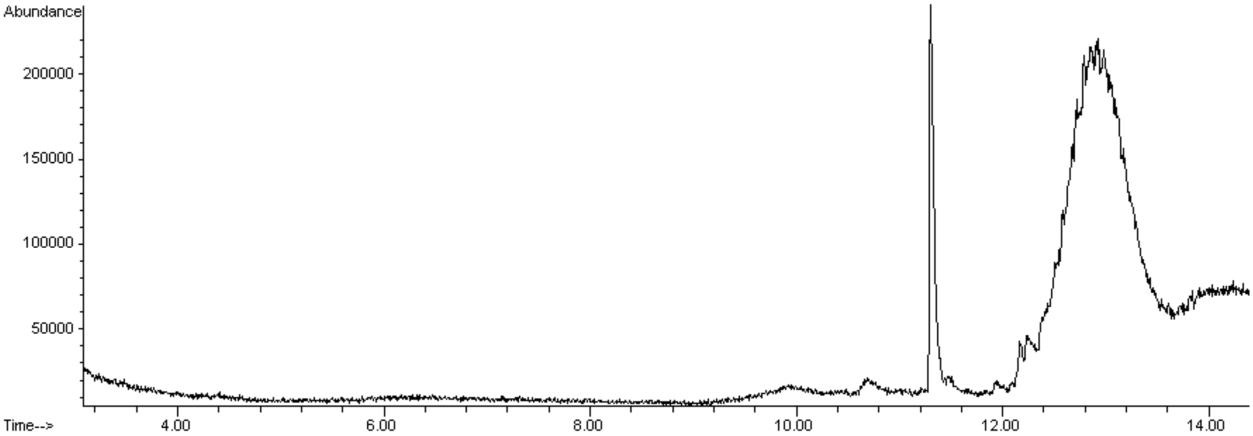
GC-MS [50-SPT]: Reaction F - 10mol% $FeCl_2$ + 10mol% Ligand **9** + 1000 ppm $Ni(acac)_2$



GC-MS [50-SPT]: Reaction G - no $FeCl_2$ + 10mol% Ligand **9** + 1000 ppm $Ni(acac)_2$



GC-MS [50-SPT]: Reaction H - 10mol% $FeCl_2$ + 10mol% Ligand **9** + 1000 ppm $CoCl_2$



GC-MS [50-SPT]: Reaction I - no $FeCl_2$ + 10mol% Ligand **9** + 1000 ppm $CoCl_2$

The addition of copper, nickel and cobalt salts to the standard reaction conditions did not improve the yield of the reaction (c.f. A, B, D, F and H). The salts of copper, nickel and cobalt in combination with ligand **9** alone did not catalyse the reductive cross-coupling reaction, although copper(II) chloride did show catalytic activity in the cross-coupling step.

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