Nickel/magnesium–lanthanum mixed oxide catalyst in the Kumada-coupling

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A new, heterogeneous, magnesium–lanthanum mixed oxide solid base-supported nickel(II) catalyst was developed. The catalyst was used successfully in the Kumada coupling of aryl halides, especially aryl bromides. The optimal reaction conditions of the coupling were determined.

The reaction of organomagnesium halides with carbonyl compounds discovered by Barbier[1] and improved by Grignard[2] has became a very important synthetic method even in industrial syntheses. A number of modifications of the original method were elaborated aiming to improve the functional group tolerance or the yield. Thus *e.g.* Kharasch[3] examined the effect of different metal salts on the coupling reaction of Grignard compounds with the weakly reactive aryl halides. He observed that in the reaction of bromobenzene and 4-bromotoluene the formation of homocoupled products was determinant. He suggested an interesting redox mechanism. Based on his considerations this reaction could only be used for the preparation of homocoupled products. He described the formation of polymer-like byproducts (terphenyl, *etc.*), too. He found that anhydrous cobalt chloride was the best catalyst.

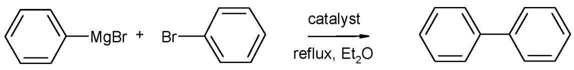
Later Kumada and his coworkers[4] described the coupling of Grignard reagents in a homogeneous, nickel complex-catalyzed reaction. Their suggestion for the reaction mechanism is more similar to the mechanism described for today's metal-catalyzed carbon–carbon coupling reactions (*e.g.* Negishi, Stille, *etc.*). It was found that nickel was the best catalyst, but if the halide was iodide, Pd was also efficient. In some cases Fe-complexes also proved to be applicable.[5] In the last years new methods were described using iron catalysts.[6]

Kumada used nickel(II) phosphine complexes in a homogeneous process with bidentate ligands such as dppe, dppp and others.[4] The advantage of these ligands is that in some cases (*e.g.* dppf, DIOP, *tert*-Leuphos) they can induce enantioselectivity.[7] Besides the phosphine compounds some other ligands were also used such as acetylacetone (Kumada–Corriu coupling).[8] Very recently Hu described the use of nickel(II) pincer complexes as good catalysts for the coupling of nonactivated aryl halides with aryl and heteroaryl nucleophiles.[9] Butadiene was also found to be a good ligand.[10]

In recent years the importance of the different carbon–carbon coupling reactions has increased significantly. Nowadays various methods are used even on an industrial scale thanks to their good yield and selectivity. The main disadvantage of these reactions is that when homogeneous catalysts are used, the metal can contaminate the product, which is unacceptable *e.g.* in pharmaceutical syntheses. This induced a considerable research effort to develop new, heterogeneous catalytic systems. Lipshutz described the use of Ni on activated charcoal (DARCO) in the Kumada coupling. He obtained good conversions even with aryl chloride, but only in the presence of an equimolar amount of anhydrous LiBr. The other disadvantage of his method is that a large amount (*ca.* 20 mol%) of triphenyl phosphine (free or polymer-bound) has to be added into the reaction mixture. Without this ligand the yield decreased significantly and a considerable amount of homocoupled product was detected.[11] Styring[12] bound a nickel chelate complex to Merrifield-resin and this modified resin was used as catalyst. The disadvantage of this method is that a great excess (3 moles) of Grignard compound is necessary to obtain a good yield. Very recently Richardson[13] examined the coupling of phenylmagnesium chloride and 4-bromoanisole using nickel(II)acetylacetonato complex supported on either polymer-bound ethylenediamine or on modified mesoporous silica. He found that the leached nickel promoted the catalysis.

Recently our research group has developed a new heterogeneous catalyst, Pd on magnesium–lanthanum mixed oxide, and applied it successfully in the Heck, Sonogashira and Suzuki reaction.[14–16] Based on these results we investigated the applicability of related, heterogeneous catalyst systems in the Kumada coupling.

The coupling of a Grignard reagent with halides can be effected without catalyst *via* nucleophilic substitution, if the halide is activated, such as allyl bromide or benzyl bromide. Alkyl halides react weakly and the reactivity, of course, further decreases towards vinyl and aryl halides. The Kumada reaction can be a useful method for the coupling of these unactivated halides. To investigate the applicability of a heterogeneous catalyst for the coupling we chose the reaction of phenylmagnesium bromide with bromobenzene (Scheme 1) as a model reaction.



Scheme 1

As it was described, the coupling can be catalyzed by different metals. Nickel has been used most frequently, but palladium, iron and other metals were also applied. Thus, we first examined the efficiency of different metals. These metals were placed onto different supports having basic properties namely Mg : Al 2 : 1 or 3 : 1 hydrotalcite (HT), Mg : La 3 : 1 mixed oxide (MgLaO), and 4 Å molecular sieve (4A).

As was expected the reaction without catalyst gave a poor yield (Table 1, entry 1), and most of this product has already been formed during the formation of the Grignard reagent. It is well known, that the commercial Grignard-reagents always contain

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Table 1 Effect of the metal and the support on the coupling of bromobenzene

Entry	Catalyst[a]	Yield (%)[b]
1	—	16
2	Pd^{2+}–MgLaO	30
3	Pd^0–MgLaO	26
4	Co^{2+}–HT 2 : 1	49
5	Cu^{2+}–MgLaO	30
6	Cu^{2+}HT 2 : 1	22
7	Cu^0–HT 2 : 1	28
8	Fe^{3+}–HT 2 : 1	<5
9	Fe^{3+}–HT 3 : 1	<5
10	Fe^{3+}–4A	<5
11	Ni^{2+}–HT 2 : 1	72
12	Ni^{2+}–HT 2 : 1 (calc.)	26
13	Ni^{2+}-4A	66
14	**Ni^{2+}–MgLaO**	**86**[c]
15	Ni^{2+}–MgO	67
16	Ni^{2+}–La_2O_3	66
17	MgLaO	18
18	anhydrous $NiCl_2$[d]	67

[a] 1 mmol metal/g support, 10 ml Et_2O, 0.2 g catalyst/10 mmol substrate, reflux. [b] Isolated yield, the purity is checked by GC-MS. [c] Using THF instead of diethyl ether the same yield was obtained. [d] 4% metal (Kharasch method)

a certain amount of coupled product as contaminant which is explained by a reaction of one Grignard compound with another.

In agreement with Kumada's statement, the best yield was obtained with nickel. Palladium, both in the form of Pd(II) and Pd(0) gave poor yield. Cobalt, which had been described by Kharasch as the best metal for this type of coupling, gave moderate yield. Copper, which is also known as efficient catalyst or co-catalyst for several coupling reactions[17] showed no high activity. Although $Fe(acac)_3$ has been described as a catalyst for the coupling, when we used iron(III) on hydrotalcite or on 4 Å molecular sieves (entries 8–10), the product was no the required biphenyl but a complex mixture was obtained. The best result was obtained with MgLa mixed oxide support (entry 14). This would suggest that – since this mixed oxide is a quite strong Lewis base – the efficiency of the support would be determined by its basicity. But in this case 4 Å molecular sieves (entry 13) which are also a strong Lewis base, should give a similar result as MgLaO. Thus the support would seem to have another effect. The simple oxides, MgO and La_2O_3 (entries 15 and 16, resp.) showed weaker activity. Calcination of Mg : Al 2 : 1 hydrotalcite impregnated with nickel chloride (Ni^{2+}–HT 2 : 1) decreased the activity of the catalyst significantly (entry 12). The MgLa mixed oxide without nickel showed no activity *e.g.* the same yield was obtained as without any additive (entry 17 *vs.* entry 1). In all of the cases, when the supports HT and MgLaO were compared with the same metal, the MgLaO proved to be more efficient. When the original Kharasch-experiment was reproduced, GC-MS investigation of the products showed the presence of higher polymeric species (entry 18) according to the mechanism proposition of Kharasch.[3]

The structure of the Ni^{2+}–MgLaO catalyst was investigated by scanning electron microscopy. The nickel is evenly distributed on the surface of the support (Fig. 1). The low intensity of chlorine (Fig. 2) possibly indicates that during the preparation of the catalyst it is not a simple surface adsorption that occurs. The nickel has exchanged probably with magnesium and been incorporated into the surface structure of the mixed oxide support, as can be seen in Fig. 1 (right). This is supported by the ICP-OES results which showed a slight decrease in the Mg : La ratio comparing the pure support and the catalyst. Additionally, the presence of chlorine and magnesium was shown in the filtrate obtained during the workup in the preparation process of the catalyst. The amount of the nickel on the support was also determined by ICP-OES and was found to be 0.8 mmol g^{-1}.

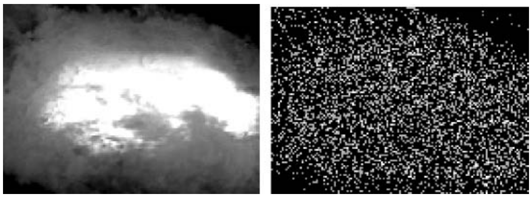


Fig. 1 SEM image of a catalyst particle (left) and distribution of the nickel on the particle (right) (magnification: 4000×).

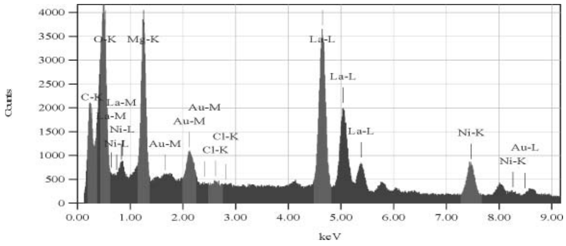


Fig. 2 Standard quantitative analysis of the catalyst.

Table 2 Effect of the amount of nickel on the coupling[a]

Entry	Nickel concentration on the catalyst/ mmol g^{-1}	Catalyst amount/g	Nickel amount/ mol%	Yield[b] (%)
1	0.8	0.2	1.6	86
2	0.4	0.2	0.8	87
3	**0.08**	**0.2**	**0.16**	**88 (88)**[c]
4	0.08	0.1	0.08	42
5	0.04	0.2	0.08	42
6	0.016	0.2	0.032	39
7	0.016	0.4	0.064	77

[a] 10 mmol substrate, 6 h. [b] Isolated yield, the purity is checked by GC-MS. [c] Reaction time: 12 h.

To avoid the contamination of the product and/or the environment, the amount of the heavy metal used in an organic synthesis should be as low as possible. Thus we examined the effect of the amount of the nickel on the coupling. As is shown in Table 2, the optimal amount of nickel was 0.16 mol%. In the cases when the yield was lower, the reaction mixture contained the unreacted starting materials. In the published experiments the amount of nickel varied between 0.3[4] and 3 mol%.[9] Thus, our catalyst requires a smaller amount of nickel for a good yield than the published methods.

The use of this type of solid catalyst system generally induces dispute over whether the reaction takes place on the solid surface or with the metal leached into the solution. We used the hot filtration test to choose from these two possibilities. Thus, after 2 h the reaction mixture was filtered, and the filtrate was examined by X-ray fluorescence. This showed that there was about 1–2 ppm nickel in the solution which might verify a capture–release mechanism. The X-ray fluorescence investigation of the isolated products showed the absence of nickel.

In the preliminary experiments the reaction time was 6 h. We examined the effect of the reaction time and found, that the yield increased significantly with the reaction time, but after 3 h it had no longer effect as is shown in Fig. 3.

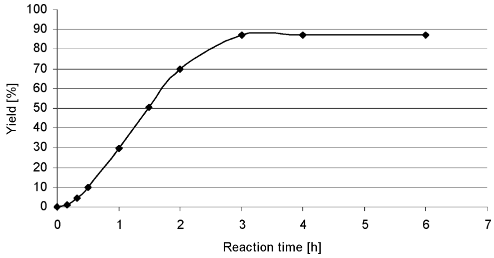
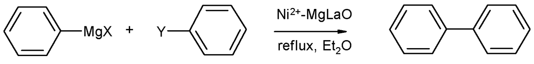


Fig. 3 Effect of the reaction time on the yield.

The nature of the coupling aryl halide influences the reactivity significantly. The reaction of different halobenzenes and phenylmagnesium halides were investigated in the presence of Ni^{2+}–MgLaO (10 mmol of each reactant, diethyl ether, reflux, 3 h, Scheme 2). The results (Table 3) show the general reactivity of the aryl halides. Nevertheless, the Y halogen plays the key role. If it is iodine, then an excellent yield can be expected. But the bromo derivative gave also good results. The chloro derivative gave a moderate yield even after a longer reaction time.

With the optimal reaction conditions we examined the scope of the cross-coupling (Scheme 3). In the reaction of phenylmagnesium bromide and *p*-bromotoluene 61% of the desired product was obtained, but the two homocoupled products, biphenyl and *p*,*p*′-bitolyl were also obtained. When the ratio of the R_1-aryl bromide : magnesium was changed to 1.3 : 1.15 in the Grignard reaction, no *p*,*p*′-bitolyl was formed, but near the 86% 4-methylbiphenyl 15% biphenyl was also obtained. Thus, this way the formation of the R_2-homocoupled product can be avoided since there is no residual magnesium in the mixture which could form a Grignard reagent from R_2-aryl halide. With this modified conditions we examined the reaction of different aryl bromides. Using higher excess of Grignard compounds the yield did not increased. The results are summarized in Table 4.

As it is shown, generally good results were obtained when the Grignard reagent was formed from bromobenzene, except when the coupling aryl halide was *o*-trifluoromethyl-bromobenzene. This latter gave a poor yield in every reaction. The Grignard reagent obtained from *p*-bromotoluene had poorer reactivity than bromobenzene. Entries 11 and 12 gave surprisingly weak results. When the reaction of *p*-tolylmagnesium bromide with *p*-bromoanisole (entry 11) was investigated by GC-MS the presence of a great amount of unreacted *p*-bromoanisole and the lack of *p*-bromotoluene showed that the formation of the Grignard compound occurred, but the coupling took place weakly.

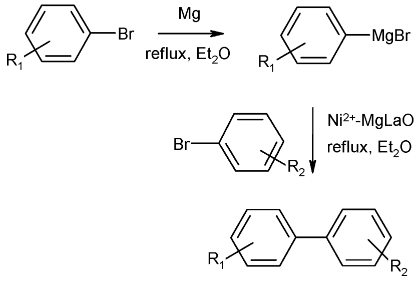


Scheme 2

Table 3 Effect of the halogen on the yield[a]

Entry	X	Y	Yield (%)
1	Br	Cl	50 (51)[b]
2	Br	Br	86
3	Br	I	99
4	I	I	94

[a] Reaction time: 6 h. [b] Reaction time: 18 h.



Scheme 3

Table 4 Results of the cross-coupling reactions[a]

Entry	R_1	R_2	Yield (%)[b]
1	H	*p*-Me	86
2	H	*o*-OMe	73
3	H	*m*-OMe	81
4	H	*p*-OMe	83
5	H	*o*-CF_3	23
6	H	*m*-CF_3	78
7	H	*p*-CF_3	84
8	*p*-Me	*o*-CF_3	25
9	*p*-Me	*m*-CF_3	69
10	*p*-Me	*p*-CF_3	29
11	*p*-Me	*p*-OMe	55
12	*p*-OMe	*p*-Me	11
13	*p*-CF_3	*m*-CF_3	21

[a] Conditions: 11.5 mmol Grignard compound, 10 mmol aryl bromide, 0.2 g Ni^{2+}–MgLaO, 10 ml diethyl ether, 3 h. [b] Isolated yield based on R_2-aryl bromide, *ca.* 15% R_1-C_6H_4–C_6H_4-R_1 was also formed which was shown by GC-MS.

Contrarily when the Grignard compound was formed from *p*-bromoanisole and this was coupled with *p*-bromotoluene (entry 12), GC-MS of the product showed the presence of a lot of anisole, which was formed from the unreacted Grignard compound during the workup of the reaction mixture. These results show that the methoxy group can inhibit the reaction, although this is not verified by the results obtained in entries 2–4.

The investigation of the crude products by GC-MS showed that the amount of other byproducts, such as phenol (formed by reaction of the Grignard compound with oxygen from the air and subsequent hydrolysis) or 2-phenylethanol (formed by a radical reaction between the Grignard reagent and the solvent diethyl ether) did not exceed 0.2% in any of the cases.

The recyclability of the catalyst was investigated in the reaction of bromobenzene and *p*-bromotoluene. Thus in the first reaction the yield obtained was 86%. The catalyst was filtered out from the mixture and after washing it with toluene and drying at 120 °C for 1 h it was reused in the same reaction. In the second run the yield obtained was 70%. The quite big decrease in the yield can be explained with the precipitation of magnesium bromide – which is formed in the reaction of necessity – onto the surface of the catalyst. Its separation from the catalyst cannot be effected easily because of its low solubility in organic solvents.

Thus a new, efficient catalytic method was elaborated for the coupling of arylmagnesium bromides or iodides with aryl halides (especially bromides) using nickel(II) on Mg–La mixed oxide as catalyst with good yield. The catalyst is easy separable from the reaction mixture, thus the nickel contamination of the product can be avoided.†

Acknowledgements

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Notes and references

† Preparation of nickel(II)/magnesium-lanthanum mixed oxide: Magnesium–lanthanum mixed oxide was prepared as described in Reference 14. This mixed oxide (3.0 g) was suspended in 300 ml of deionized water and 0.714 g nickel(II)-chloride hexahydrate was added into the mixture. The suspension was stirred at room temperature for 24 h, then the light greenish solid was filtered out, washed with deionized water and dried at 120 °C for 4 h. The catalyst was stored under argon atmosphere. Before the experiments it was dried at 100 °C for 1 h. The other catalysts were prepared analogously.

Reaction of phenylmagnesium bromide with bromobenzene: 0.25 g (10 mmol) of magnesium turnings were added to 10 ml of diethyl ether, then 1.06 ml (1.57 g, 10 mmol) of bromobenzene was added to the mixture under vigorous stirring. After the complete dissolution of magnesium 0.2 g of the catalyst and then another 1.06 ml of bromobenzene were added and the mixture was stirred for 6 h under reflux. Then the mixture was cooled, diluted with ether, the solid was filtered out, washed with ether or with toluene, the filtrate was treated with 10 ml of water, the layers were separated, the aqueous was washed with ether, the combined organic phase was dried over anhydrous sodium sulfate, the solvent was evaporated. The residue was examined by GC-MS.

General procedure of the cross-coupling: 0.28 g (11.5 mmol) of magnesium turnings were added to 20 ml of diethyl ether, then 13 mmol of aryl bromide was added to the mixture under vigorous stirring. After the complete dissolution of magnesium half the amount of the solvent was evaporated, to the residue 0.2 g of the catalyst and then 10 mmol of the coupling aryl bromide were added and the mixture was stirred for 3 h under reflux. Then the mixture was cooled, diluted with ether, the solid was filtered out, washed with ether or with toluene, the filtrate was treated with 10 ml of water, the layers were separated, the aqueous layer was washed with ether, the combined organic phase was dried over anhydrous sodium sulfate, the solvent was evaporated. The residue was purified or examined by GC-MS.

Selected spectroscopic data:

Biphenyl: white crystals, m.p.: 66–67 °C (hexane) (lit.: 67–68 °C[18]); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.27–7.58 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 127.1, 127.2, 128.6, 141.1. Anal. Calcd. for $C_{12}H_{10}$: C 93.51, H 6.49%, found: C 93.46, H 6.53%.

4-Methyl-biphenyl: white crystals, m.p.: 42–43 °C (diethyl ether) (lit.: 44–46 °C[19]); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.38 (s, 3H), 7.24–7.41 (m, 5H), 7.48–7.57 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 21.7, 127.2, 129.3, 129.8, 137.2, 139.0, 141.4. Anal. Calcd. for $C_{13}H_{12}$: C 92.86, H 7.14%, found: C 93.01, H 7.08%.

2-Methoxy-biphenyl:[20] colorless oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 3.80 (s, 3H), 7.23–7.61 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 55.2, 111.5, 120.3, 127.0, 127.9, 128.8, 129.9, 130.7, 130.9, 138.4, 156.5; MS m/z(%): 184 (M^+, 100), 169 (54), 141 (51). Anal. Calcd. for $C_{13}H_{12}O$: C 84.78, H 6.52%, found: C 84.86, H 6.50%.

3-Methoxy-biphenyl:[21] yellowish oil, ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 55.3, 112.8, 113.0, 119.8, 127.3, 127.5, 128.9, 129.9, 141.2, 142.9, 160.0; MS m/z(%): 184 (M^+, 100), 154 (29), 141 (32), 115 (36.5). Anal. Calcd. for $C_{13}H_{12}O$: C 84.78, H 6.52%, found: C 84.78, H 6.46%.

4-Methoxy-biphenyl:[22] white crystals, m.p. 89–90 °C (lit.: 90–91 °C[23]); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 3.85 (s, 3H), 7.23–7.56 (9H, m, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 55.4, 114.5, 126.6, 126.8, 127.9, 128.8, 133.9, 141.0, 159.5; MS m/z(%): 184 (M^+, 100), 169 (54), 141 (61), 115 (43). Anal. Calcd. for $C_{13}H_{12}O$: C 84.78, H 6.52%, found: C 84.76, H 6.54%.

2-Trifluoromethyl-biphenyl:[24] colorless liquid, ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.28–7.34 (m, 3H), 7.36–7.49 (m, 4H), 7.51–7.59 (m, 1H), 7.74 (d, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 124.3 (q), 125.9, 127.4, 127.6, 127.7, 128.6, 129.2, 131.2, 132.1, 140,1, 141.4; MS m/z(%): 222 (M^+, 100), 201 (34), 153 (9). Anal. Calcd. for $C_{13}H_9F_3$: C 70.27, H 4.05%, found: C 70.12, H 3.89%.

3-Trifluoromethyl-biphenyl:[25] yellowish liquid, ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.36–7.67 (m, 6H), 7.76 (d, 1H), 7.81 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 124.0 (q), 127.3, 127.4, 128.2, 129.0, 129.1, 129.4, 130.6 ppm; MS m/z(%): 222 (M^+, 100), 203 (6.1), 201 (13), 153 (24.7). Anal. Calcd. for $C_{13}H_9F_3$: C 70.27, H 4.05%, found: C 70.21, H 3.96%.

4-Trifluoromethyl-biphenyl: white solid, m.p. 69–70 °C (lit.: 70–70,5 °C[26]), ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 125.8 (q), 127.2, 127.4, 127.5, 128.3, 128.8, 129.1, MS m/z(%): 222 (M^+, 100), 203 (7.9), 153 (22.8). Anal. Calcd. for $C_{13}H_9F_3$: C 70.27, H 4.05%, found: C 70.20, H 4.08%.

4-Methyl-2′-(trifluoromethyl)-biphenyl:[27] colorless liquid, ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.43 (s, 3H), 7.21–7.25 (m, 4H), 7.33 (d, 1H), 7.46 (t, 1H), 7.56 (t, 1H), 7.78 (d, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 21.2, 124.3 (q), 126.8, 127.4, 128.6, 128.8, 131.3, 132.3, 137.1, 137.5, 141.4; MS m/z(%): 236 (M^+, 100), 201 (21), 165 (26), 91 (15). Anal. Calcd. for $C_{14}H_{11}F_3$: C 71.19, H 4.61%, found: C 71.28, H 4.57%.

4-Methyl-3′-(trifluoromethyl)-biphenyl:[28] colorless liquid, ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.41 (s, 3H), 7.28 (d, 2H), 7.46–7.64 (m, 4H), 7.74-7.81 (m, 1H), 7.85 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 21.2, 123.8 (q), 124.3, 127.2, 129.0, 129.8, 130.3, 131.5, 137.8, 141.6; MS m/z(%): 236 (M^+, 100), 217 (6), 165 (31), 91 (13). Anal. Calcd. for $C_{14}H_{11}F_3$: C 71.19, H 4.61%, found: C 71.05, H 4.73%.

4-Methyl-4′-(trifluoromethyl)-biphenyl:[29] colorless solid, m.p. 120 °C (lit.: 121 °C[28]), ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.45 (s, 3H), 7.28 (m, 2H), 7.53 (m, 2H), 7.68 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 21.1, 125.6 (q), 125.8, 127.2, 127.3, 129.2, 129.7, 137.1, 138.3, 144.6; MS m/z(%): 236 (M^+, 100), 217 (7), 165 (40), 152 (13), 91 (11). Anal. Calcd. for $C_{14}H_{11}F_3$: C 71.19, H 4.61%, found: C 71.25, H 4.59%.

4-Methoxy-4′methyl-biphenyl: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.39 (s, 3H), 3.83 (s, 3H), 7.01 (m, 2H), 7.23 (m, 2H), 7.48 (m, 2H), 7.53 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 21.1, 55.3, 114.3, 126.6, 127.7, 129.5, 133.7, 136.4, 138.1, 158.7; MS m/z(%): 198 (M^+, 100), 183 (56), 128 (13), 77 (7). Anal. Calcd. for $C_{14}H_{14}O$: C 84.85, H 7.07%, found: C 84.75, H 6.99%.

3,4′-Bis-(trifluoromethyl)-biphenyl: MS m/z(%): 290 (M^+, 100), 271 (22), 241 (13), 221 (7), 219 (6), 201 (20), 152 (16), 145 (10), 120 (6), 95 (8). Anal. Calcd. for $C_{14}H_8F_6$: C 57.93, H 4.76%, found: C 57.75, H 4.56%.

1 P. Barbier, *C. R. Acad. Sci.*, 1899, **128**, 110–111.
2 V. Grignard, *Compt. Rend.*, 1900, **130**, 1322.
3 M. S. Kharasch and E. K. Fields, *J. Am. Chem. Soc.*, 1941, **63**, 2316–2320.
4 K. Tamao, K. Sumitani and M. Kumada, *J. Am. Chem. Soc.*, 1972, **94**, 4374–4376.
5 A. Fürstner and A. Leitner, *Angew. Chem., Int. Ed.*, 2002, **41**, 609–612.
6 A. Leitner, in *Iron Catalysis in Organic Chemistry: Reactions and Applications*, (Ed.: B. Plietker), Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, 2008, pp. 147–172.
7 T. Hayashi, M. Konishi, M. Fukushima, K. Kanehira, T. Hioki and M. Kumada, *J. Org. Chem.*, 1983, **48**, 2195–2202.
8 R. J. P. Corriu and J. P. Masse, *J. Chem. Soc., Chem. Commun.*, 1972, 144.
9 O. Vechorkin, V. Proust, and X. Hu, *J. Am,. Chem. Soc.* 2009, 10.1021/ja9027378.
10 J. Terao, H. Watanabe, A. Ikumi, H. Kuniyasu and N. Kambe, *J. Am. Chem. Soc.*, 2002, **124**, 4222.
11 (*a*) B. H. Lipshutz, T. Tomioka, P. A. Blomgren and J. A. Sclafani, *Inorg. Chim. Acta*, 1999, **296**, 164–169; (*b*) B. H. Lipshutz, S. Tasler, W. Chrisman, B. Spliethoff and B. Tesche, *J. Org. Chem.*, 2003, **68**, 1177–1189.
12 P. Styring, C. Grindon and C. M. Fisher, *Catal. Lett.*, 2001, **77**, 219–225.
13 J. M. Richardson and C. W. Jones, *J. Mol. Catal. A: Chem.*, 2009, **297**, 125–134.
14 A. Cwik, Z. Hell and F. Figueras, *Adv. Synth. Catal.*, 2006, **348**, 523–530.

15 A. Cwik, Z. Hell and F. Figueras, *Tetrahedron Lett.*, 2006, **47**, 3023–3026.
16 A. Cwik, Z. Hell and F. Figueras, *Org. Biomol. Chem.*, 2005, **3**, 4307–4309.
17 Th. W. Bell, L. Y. Hu and S. V. Patel, *J. Org. Chem.*, 1987, **52**, 3847–3850.
18 M. Uchiyama, T. Suzuki and Y. Yamazaki, *Chem. Lett.*, 1983, 1165–6.
19 Y. Endo, K. Shudo and T. Okamoto, *J. Am. Chem. Soc.*, 1982, **104**, 6393.
20 J. P. Wolfe, R. A. Singer, B. H. Yang and S. L. Buchwald, *J. Am. Chem. Soc.*, 1999, **121**, 9550.
21 P. D. Stevens, J. Fan, H. M. R. Gardimalla, M. Yen and Y. Gao, *Org. Lett.*, 2005, **7**, 2085.
22 M. L. Kantam, M. Roy, S. Roy, B. Sreedhar, S. S. Madhavendra, B. M. Choudary and R. Lal De, *Tetrahedron*, 2007, **63**, 8002.
23 C. Desmarets, R. Omar-Amrani, A. Walcarius, J. Lambert, B. Champagne, Y. Fort and R. Schneider, *Tetrahedron*, 2008, **64**, 372–381.
24 D. Zim, A. S. Gruber, G. Ebeling, J. Dupont and A. L. Monteiro, *Org. Lett.*, 2000, **2**, 2881.
25 Z.-Y. Tang and Q.-S. Hu, *J. Am. Chem. Soc.*, 2004, **126**, 3058.
26 T. Mino, Y. Shirae, T. Saito, M. Sakamoto and T. Fujita, *J. Org. Chem.*, 2006, **71**, 9499–9502.
27 K. Fuchibe and T. Akiyama, *J. Am. Chem. Soc.*, 2006, **128**, 1434–1435.
28 L. Ackermann and A. Althammer, *Org. Lett.*, 2006, **8**, 3457–3460.
29 A. H. Roy and J. F. Hartwig, *J. Am. Chem. Soc.*, 2003, **125**, 8704–8705.