Turkish Journal of Chemistry

http://journals.tubitak.gov.tr/chem/

Review Article

Turk J Chem
(2015) 39: 1158 – 1170

doi:10.3906/kim-1507-73

Contribution of heterobifunctional ligands to transition metal-catalysed C–C coupling reactions

Agnès LABANDE[1,2,*], **Eric DEYDIER**[1,2,3,*], **Eric MANOURY**[1,2,*], **Jean-Claude DARAN**[1,2], **Catherine AUDIN**[3], **Rinaldo POLI**[1,2,4]

[1]CNRS, LCC (Laboratoire de Chimie de Coordination), Toulouse, France
[2]University of Toulouse, Toulouse, France
[3]IUT A Paul Sabatier, Department of Chemistry, Castres, France
[4]Institut Universitaire de France, Paris, France

Received: 24.07.2015 • **Accepted/Published Online:** 10.09.2015 • **Printed:** 25.12.2015

Abstract: In this account the authors' latest results in C–C coupling catalysis are reviewed. First, an efficient catalytic system for the Kumada–Tamao–Corriu coupling reaction based on NHC-phosphine (NHC = N-heterocyclic carbene) nickel complexes is presented. Then the use of palladium complexes of chiral ferrocenyl NHC-phosphines in the asymmetric Suzuki–Miyaura coupling reaction is reported. High catalytic activities and moderate enantioselectivities (ee up to 46%) were obtained. Chiral ferrocenyl phosphine–ethers were also tested in the asymmetric Suzuki–Miyaura reaction yielding good activities and moderate enantioselectivities (ee up to 37%). Finally, the original synthesis of a ferrocenyl rhodium(III) complex and its successful use as catalyst for a C–C coupling reaction via C–H activation of 2-phenylpyridine is presented.

Key words: Chiral ferrocenyl ligands, NHC ligands, P,O ligands, palladium, Kumada–Tamao–Corriu reaction, Suzuki–Miyaura cross-coupling, asymmetric catalysis

1. Introduction

Cross-coupling reactions have become one of the most powerful reactions to access functionalised aromatics and are involved in key steps in the synthesis of molecules for pharmaceutical and agrochemical applications.[1–4] Many transition metals have been used to catalyse these reactions, aided by a great variety of ligands ranging from simple, commercial phosphines to complex custom-made molecules. It is known that the nature of the ligand strongly determines the activity and the selectivity of the catalyst. Therefore, its design is of prime importance for a given application, particularly when asymmetric catalysis is involved. Ligand design directed toward catalytic applications has been a major focus in our group for many years, particularly concerning heterobifunctional ligands that can produce robust yet very active catalysts by the careful choice of their coordinating units and that can be prepared easily in enantiopure form when asymmetric induction is required.[5–9] In this area, chiral phosphines have played a significant role and, among the numerous phosphine ligands reported to date, ferrocenyl phosphines constitute a distinct class of ligands attracting increasing interest.[10–12] More recently, N-heterocyclic carbene (NHC) ligands have also emerged as powerful ligands for catalysis and asymmetric catalysis.[13,14]

*Correspondence: agnes.labande@lcc-toulouse.fr, eric.deydier@iut-tlse3.fr, eric.manoury@ lcc-toulouse.fr

We have recently developed promising ferrocenyl and NHC ligands as racemic mixtures or in enantiomerically pure forms when chiral and started investigating their efficiency in catalysis. Cross-coupling reactions naturally came to us as interesting targets, as room for improvement was available in terms of catalyst design, particularly for challenging reactions such as the asymmetric Suzuki–Miyaura cross-coupling of hindered aromatics[15–17] or the direct C–H functionalisation of aryl substrates.[18] Our first objective, however, was the study of the nickel-catalysed Kumada–Tamao–Corriu (KTC) reaction for the coupling of less reactive but more available aryl chlorides with arylmagnesium halides.

2. Kumada–Tamao–Corriu with NHC-phosphine ligands

When our investigations started in 2004, most catalysts were based on phosphine ligands, which are air-sensitive and often gave poorly stable catalysts.[19,20] In 1994, Herrmann first showed the efficiency of N-heterocyclic carbene ligands in catalysis, and more particularly in palladium-catalysed cross-coupling reactions.[21,22] Later, the same authors described catalytic systems based on $Ni(acac)_2$ and imidazolium salts, precursors of N-heterocyclic carbenes (**A**, Figure 1), for the KTC reaction.[23] The NHC/Ni catalysts, generated in situ by deprotonation of the imidazolium salts, proved very active for the coupling of more demanding (hetero)aryl chlorides with arylmagnesium halides at room temperature and more selective than palladium-based NHC or phosphine catalysts for similar substrates.

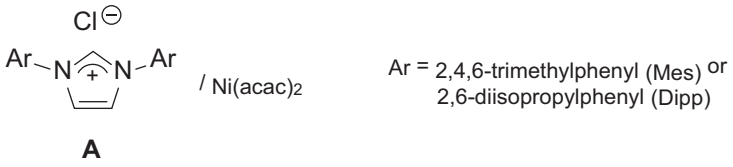

Figure 1. First NHC ligands used in the nickel-catalysed Kumada–Tamao–Corriu reaction.[23]

On these premises, we developed heterobifunctional ligands bearing one N-heterocyclic carbene donor, capable of creating a very strong bond with the metal centre, and one phosphine donor that possesses different stereoelectronic properties.[24,25] We envisaged that the association of these two donors in a chelating ligand could give robust yet active catalysts, and that the different stereoelectronic environment would enforce a different *trans* influence on the incoming substrates, thus bringing interesting selectivity issues.

The synthesis of several phosphine-imidazolium salts, differing by the tether length as well as the imidazolium N-substituent, was thus developed and **1a**–**d** (Figure 2) were obtained in good yields in 3 steps from substituted imidazoles. We envisioned that the phosphine-imidazolium salts **1a**–**b**, with a tether length of two carbons, would give the most active catalysts since they would form 6-membered metallacycles with nickel, similar to the efficient Ni/dppp system. The reaction of these salts with nickel(II) precursors gave air-stable zwitterionic complexes **2a**–**d**, with coordination of the phosphine only. All complexes are paramagnetic and possess a distorted tetrahedral geometry. Upon deprotonation of the imidazolium moiety and generation of the N-heterocyclic carbene, however, the resulting complexes are diamagnetic and likely adopt a square-planar geometry around the metal. An NMR monitoring of the deprotonation of **2a** by methyl lithium confirmed the presence of two different nickel NHC-phosphine complexes, attributed to a monomeric and a dimeric species.

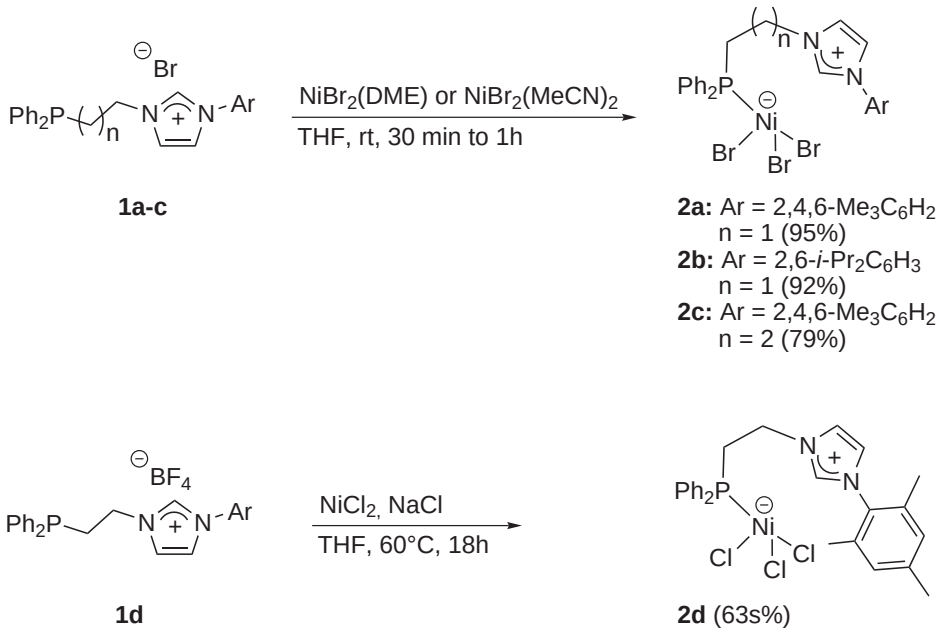

Figure 2. Synthesis of the phosphine-NHC nickel complexes used in the Kumada–Tamao–Corriu reaction.[24,25]

The activity of all zwitterionic complexes in the KTC coupling was evaluated in the presence of a range of (hetero)aryl chlorides and a sterically demanding aryl bromide (Table 1). The reactions were run in the presence of 3 mol% catalyst at room temperature in THF and were stopped after 18 h to allow for a direct comparison of activities with the different substrates. The N-heterocyclic carbene complexes were presumably generated at the start of the reaction, as the colour of the reaction mixture changed from blue-green to brown-orange upon addition of the Grignard reagent.

Table 1. KTC reaction of aryl chlorides with arylmagnesium halides catalysed by complexes **2a**–**c**.

Entry	R^1	E	R^2	X	Cat. **2a**[b]	Cat. **2b**[b]	Cat. **2c**[b]	IPr/Ni(acac)$_2$[c]
1	H	N	H	Cl	> 99	> 99	> 99	> 99
2	4-CF_3	C	H	Cl	37	53	29	96
3	4-CH_3	C	H	Cl	86	96	63	81
4	4-OCH_3	C	H	Cl	95	92	80	71
5	2-CH_3	C	H	Cl	78	82	23	73
6	bromomesitylene	C	H	Cl	4	3	7	5
7	H	N	4-OCH_3	Br	> 99	> 99	> 99	> 99
8	4-CF_3	C	4-OCH_3	Br	36	33	42	> 99
9	H	C	4-OCH_3	Br	99	98	76	93
10	4-CH_3	C	4-OCH_3	Br	92	87	89	88
11	2-CH_3	C	4-OCH_3	Br	48	87	12	77

[a] Conditions: 1.0 eq aryl halide, 1.5 eq aryl Grignard, 3 mol% **1a**–**c**, THF, 25 °C, t = 18 h. [b] GC yield using diethyleneglycol-di-n-butylether as the internal standard. [c] Reference 23.

The nature of the halogen on the nickel centre did not prove important as similar yields of 4-methoxybiphenyl were obtained with complexes **2a** and **2d** (not detailed in Table 1). No noticeable influence of the aryl substituent borne by the NHC was observed since complexes **2a** (Ar = Mes) and **2b** (Ar = Dipp) showed

similar activities. However, complex **2b** was slightly more selective than **2a** in many cases. The presence of the phosphine did not prove detrimental as both complexes showed an equal or slightly better activity than the $Ni(acac)_2$/IPr system described by Herrmann, and they even showed an improved selectivity for the heterocoupling product in most cases. Two exceptions were observed with bulky bromomesitylene (entry 6) and with p-chloro(trifluoromethyl)benzene (entries 2 and 8), where conversions were low. In the latter cases, the problem appeared closely related to the simultaneous presence of a CF_3 group on the substrate and a phosphine in the ligand system, showing one limitation of our heterobifunctional ligand compared to Herrmann's monodentate NHC. Finally, as expected, the presence of a seven-membered cycle in the case of complex **2c** slowed the reaction down in most cases but not all (entries 6, 8, and 10).

One major drawback of our systems, as with all in situ generated catalysts, is the uncertain nature of the species that truly catalyses the reaction. However, we can assume that the two nickel NHC-phosphine complexes observed by NMR after deprotonation with methyllithium (*vide supra*) correspond to the species generated after addition of the Grignard reagent, although we do not know the relative activity of the monomeric versus the dimeric species.

Due to the high activity and high selectivity of these complexes for the cross-coupling of aryl chlorides with arylmagnesium halides, we can assert that the choice of a bidentate NHC-phosphine ligand was well adapted and their potential for the coupling of other, more challenging substrates should be investigated further. [26,27]

3. Asymmetric Suzuki–Miyaura reaction for the synthesis of axially chiral biaryls

The asymmetric version of the palladium-catalysed Suzuki–Miyaura cross-coupling reaction has only been developed in the last 15 years because of the difficulty of finding efficient catalysts enabling the coupling of very hindered substrates. Indeed, the axial chirality of the biaryl products is induced by the restricted rotation around the aryl–aryl bond (so-called atropisomerism) and to exhibit such chirality there must be at least three ortho substituents about the biaryl axis. Atropisomerism is encountered for instance in a class of chiral ligands frequently used in asymmetric catalysis, such as BINAP, in chiral organocatalysts like the TRIP-type chiral Brønsted acids, but also in natural products like Vancomycin (Figure 3), underlining the need to develop efficient strategies toward their synthesis in optically pure form.

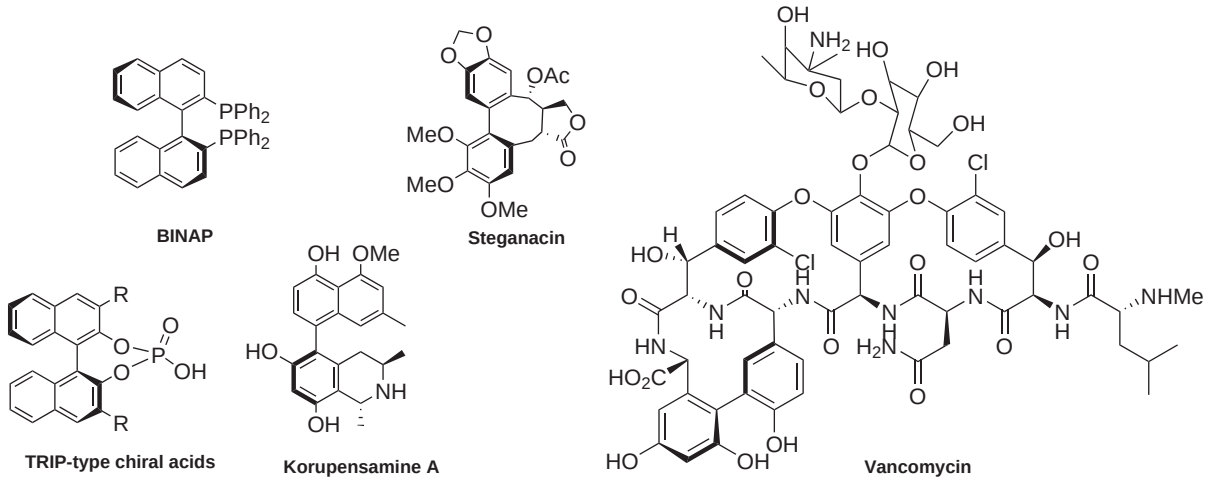

Figure 3. Examples of products containing a chiral biaryl unit.

Buchwald[28,29] and Cammidge[30,31] almost simultaneously reported the first examples of the enantioselective Suzuki–Miyaura cross-coupling reaction in 2000 and a wide range of catalytic systems has been reported since. However, as underlined in recent reviews, even if excellent activities and enantioselectivities ($>98\%$) have been reported for some systems, no ligand or catalyst has allowed reaching high levels of enantioselectivities for a large range of substrates.[10–12] Some trends emerged nonetheless in terms of ligand design, as it was shown that bulky, electron-rich ligands allowed stabilising very reactive 14e- palladium species. Two classes of chiral ligands were consistently used and proved their efficiency, i.e. ligands based on an atropisomeric biaryl backbone and planar chiral ferrocenyl ligands. In this last category, various P,P, P,N, P,O, or P chiral ferrocenyl ligands (Figure 4) have been synthesised by different groups and used with different levels of success for this reaction.[30–37]

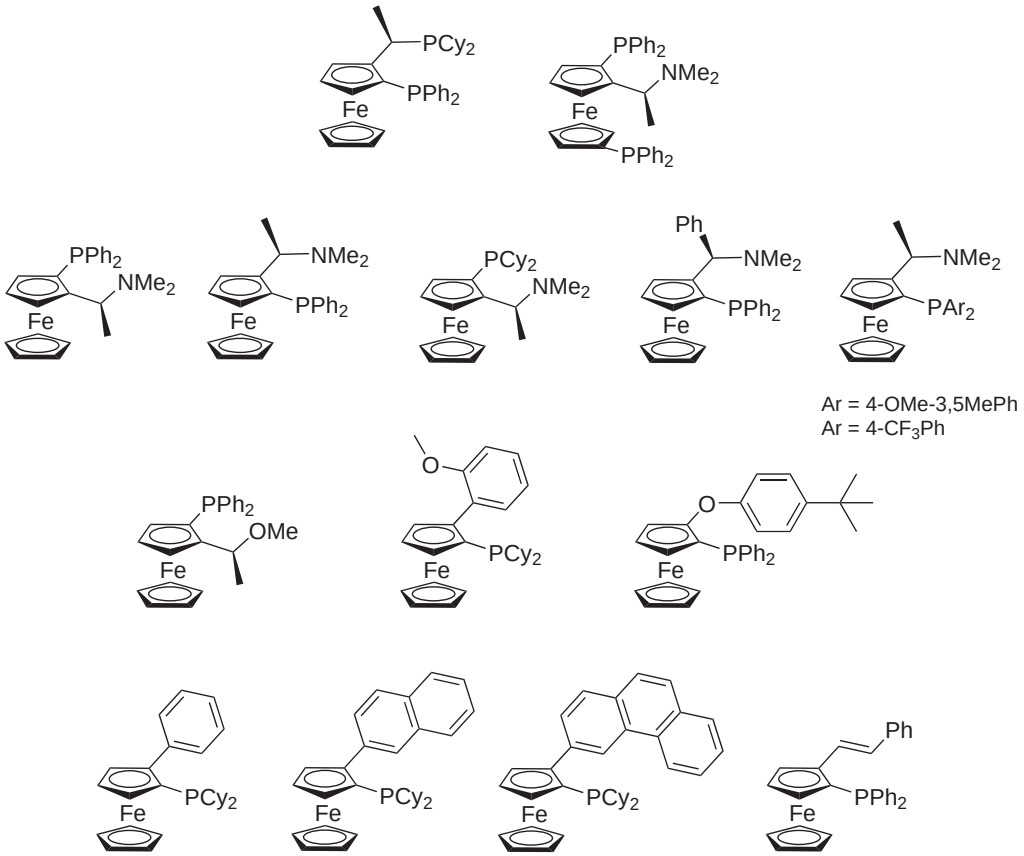

Figure 4. Examples of P,P, P,N, P,O, and P chiral ferrocenyl ligands used for asymmetric Suzuki–Miyaura reaction.

Our group has expertise in the synthesis of planar chiral ferrocenyl ligands for various catalytic applications[5–9] and we thus envisioned that we could build on this to design new ligands for the asymmetric Suzuki–Miyaura reaction. We considered two different approaches for the synthesis of the chiral ligands: our experience in the synthesis of functionalised N-heterocyclic carbenes prompted us to develop a chiral version of the strongly σ-donating NHC-phosphine ligand;[38,39] on the other hand, bulky monodentate or bidentate hemilabile ligands are efficient for this reaction, and therefore ferrocenyl P,O ligands were also evaluated.[40] Both types of ligands are based on the relatively inexpensive, commercial reagent N,N-dimethylaminomethylferrocene, whereas most other chiral ligands based on the ferrocene backbone are accessible starting from Ugi's amine. They were

prepared in a two-step synthesis from 2-thiodiphenylphosphino(hydroxymethyl) ferrocene, **3** (Figure 5). This precursor can be prepared in multigram quantities and isolated either as a racemic mixture or in each one of the two enantiomerically pure forms, giving direct access to planar chiral ligands of either absolute configuration.[41] Its functionalisation is performed in a one-pot process by successive additions of a strong acid (HBF_4) and the appropriate imidazole (Im), benzimidazole (BIm) or alcohol reagent.

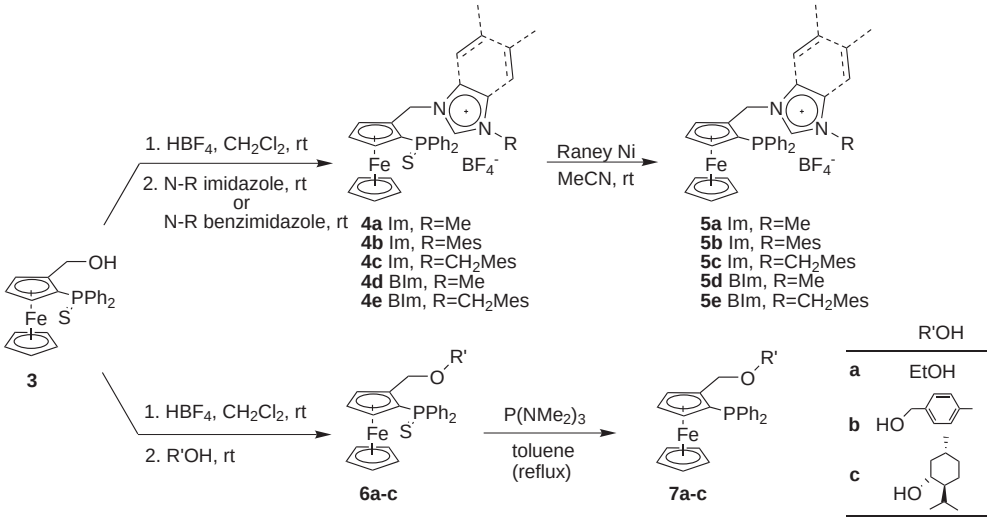

Figure 5. Synthesis of chiral phosphine-imidazolium proligands **5a**–**5e** and chiral phosphine-ether ligands **7a**–**7c**.

3.1. Catalytic application of P,NHC bidendate ligands

The use of these ligands necessitates first to synthesise and isolate the palladium catalyst as the in situ formation of the latter is not well controlled. The complexes were prepared in moderate to good yields (31%–75%) from two palladium precursors: $PdCl_2(MeCN)_2$ or $PdCl_2(PhCN)_2$ led to the neutral complexes **8** while $[Pd(allyl)Cl]_2$ gave the cationic complexes **9** (Figure 6). They have been fully characterised by NMR, mass spectrometry, and X-ray diffraction.

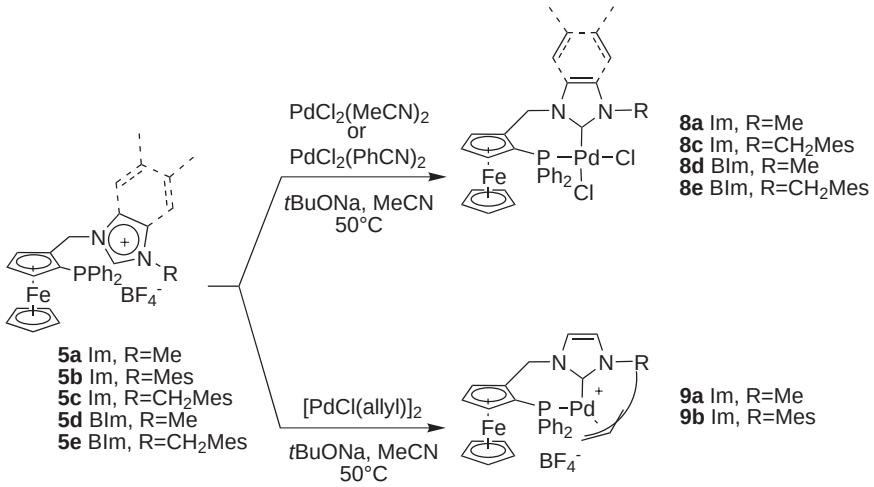

Figure 6. Synthesis of chiral phosphine-NHC palladium complexes **8a**, **8c**–**8e**, and **9a**–**9b**.

Preliminary catalytic tests were carried out for the coupling between aryl bromide and phenylboronic acid with the racemic complexes in order to assess the catalyst activity and to optimise the reaction conditions. Toluene, K_2CO_3, and 0.1–0.5 mol% catalyst were chosen respectively as solvent, base, and catalyst loading for the subsequent asymmetric coupling of binaphthalene compounds (Figure 7; Table 2). The reaction time was

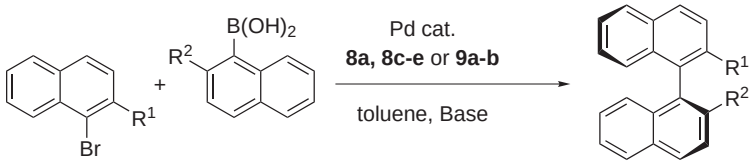

Figure 7. Asymmetric Suzuki–Miyaura coupling reaction of naphthalene derivatives.

Table 2. Asymmetric Suzuki–Miyaura reaction between naphthyl bromides and naphthylboronic acids using P-NHC ligands.[a]

Entry	Pd cat. (mol%)	R^1	R^2	T (°C)	Reaction time (h)	% Yield[b]	% ee[c]
1	**8a**-(*S*) (0.5)	H	Me	40	24	0	-
2	**8a**-(*R*) (0.1)	Me	H	70	24	89	38
3	**8a**-(*R*) (0.5)	Me	H	40	8	57	39
4	**8a**-(*S*) (0.5)	Me	H	40	24	88	40 (*S*)
5	**8a**-(*R*) (0.5)	Me	H	40	24	88	42 (*R*)
6	**8c**-(*S*) (0.5)	Me	H	40	24	58	46 (*S*)
7	**8d**-(*S*) (0.5)	Me	H	40	24	48	9 (*S*)
8	**8e**-(*S*) (0.5)	Me	H	40	24	47	37 (*S*)
9	**9a**-(*S*) (0.5)	Me	H	40	24	0	-
10	**9b**-(*S*) (0.5)	Me	H	40	24	86	19
11	**8a**-(*R*) (0.1)	OMe	H	70	24	86	33
12	**8a**-(*S*) (0.5)	OMe	H	40	24	95	35 (*R*)
13	**8a**-(*R*) (0.5)	OMe	H	40	24	93	33 (*S*)
14	**8c**-(*S*) (0.5)	OMe	H	40	24	65	31 (*R*)
15	**8d**-(*S*) (0.5)	OMe	H	40	24	54	17 (*S*)
16	**8e**-(*S*) (0.5)	OMe	H	40	24	57	22 (*R*)
17	**9a**-(*S*) (0.5)	OMe	H	40	24	30	28
18	**9b**-(*S*) (0.5)	OMe	H	40	24	82	< 2
19	**8a**-(*R*) (0.1)	OEt	H	70	24	89	30
20	**8a**-(*S*) (0.5)	OEt	H	40	24	95	23 (*R*)
21	**8a**-(*R*) (0.5)	OEt	H	40	24	92	24 (*S*)
22	**8c**-(*S*) (0.5)	OEt	H	40	24	22	26 (*R*)
23	**8d**-(*S*) (0.5)	OEt	H	40	24	65	13 (*S*)
24	**8e**-(*S*) (0.5)	OEt	H	40	24	62	23 (*R*)
25	**8e**-(*S*) (2.0)	OEt	H	40	24	54	28 (*R*)
26	**9a**-(*S*) (0.5)	OEt	H	40	24	14	10
27	**9b**-(*S*) (0.5)	OEt	H	40	24	0	-
28	**8a**-(*S*) (0.5)	$P(O)(OEt)_2$	H	40	24	0	-
29	**8c**-(*S*) (0.5)	$P(O)(OEt)_2$	H	40	24	0	-
30	**8d**-(*S*) (0.5)	$P(O)(OEt)_2$	H	40	24	0	-
31	**8e**-(*S*) (0.5)	$P(O)(OEt)_2$	H	40	24	0	-

[a] Reagents and conditions: naphthyl bromide (1.0 equiv), boronic acid (1.2 equiv), Pd cat., K_2CO_3 (2.4 equiv), toluene. [b] Isolated yield. [c] Determined by HPLC with a Chiracel-OJ column. [d] The commercial 1-bromo-2-methylnaphthalene contains ca. 6% of 2-methylnaphthalene.

fixed at 24 h in order to maximise conversions even if complex **8a** (0.1 mol%) was found to give 83% yield of biaryl after only 1 h at 70 °C.

As observed by numerous research groups, the reaction is very sensitive to the nature of R^1 and R^2 substituents as no reaction was observed when R^1 = $P(O)(OEt)_2$ (entries 28–31) or R^2 = Me (entry 1). Moderate to good yields were obtained with neutral complexes (**8a**–**e**) whereas cationic allyl complexes (**9a**–**b**) appeared to be less active and selective under the same conditions. These complexes (**9a**–**b**) seemed to decompose during the reaction as a black precipitate, probably nanoparticles,[42–44] was observed in the reaction media. This decomposition may explain the lower activity and selectivity observed for the **9a**–**b** catalysts. Another relevant observation is that increasing the catalyst steric hindrance led to decreased activity. This is expected, as steric hindrance lowers the reagents accessibility to the catalytic centre. However, we did not observe any ee improvement upon lowering the temperature from 70 °C to 40 °C (entries 2 and 5, 11, and 12, or 19 and 20). The enantioselectivity seemed unaffected by catalyst concentration and reaction time (entries 2 and 3), suggesting that the active species remains unchanged throughout the reaction. Finally, as expected, similar enantioselectivity was observed with the two enantiomers of opposite configuration (entries 4 and 5, 12 and 13, 20 and 21). One reason for the moderate levels of enantioselectivity may be the strongly coordinating nature of the ligands. Indeed, Buchwald et al. already observed that the use of diphosphine BINAP furnished the expected binaphthyls with lower ees than the corresponding P,N ligand KenPhos.[28] Similarly, the P,N ferrocenyl ligand PPFA used by Cammidge et al. showed a high selectivity whereas JosiPhos was totally inefficient.[31] The use of a mixed NHC,N ligand may therefore be an interesting alternative to consider.

3.2. Catalytic application of P,O bidendate ligands

According to a previously optimised protocol on the coupling between aryl bromides and phenylboronic acid, the reactions were carried out with caesium carbonate as base, $Pd_2(dba)_3$ (1.1 mol%) as metal precursor, and 1.2 mol% of ligand (**7a**–**c**). Contrary to the catalytic reactions with P-NHC ligands, the catalysts were generated in situ in the present case. All reactions were carried out in a low polarity solvent (toluene) to favour the coordination of both phosphorus and oxygen atoms (bidendate coordination) of the ligand for a better chirality transfer. As the temperature may be also crucial for high enantioselectivity, activity and selectivity were monitored (kinetics) for each ligand (**7a**–**c**) at three different temperatures (40, 50, and 60 °C).

As expected, the reaction rate increased with temperature whatever ligand was used. One can also note the influence of ligand steric hindrance on catalytic activity. The reaction rates are lower with the more sterically hindered benzyl- and "menthol"-substituted ligands **7b**-(*R*) and **7c**-(*R*) than with the less hindered ethyl-substituted **7a** (Table 3). However, the activity remains good, as almost 90% conversions are still observed after only 1 h at 60 °C with **7b**-(*R*) and **7c**-(*R*) (vs. 30 min for **7a**). The ee of the cross-coupling product increased, as expected, when the reaction temperature was decreased for ligand **7c** but no significant temperature effect was observed with ligand **7b**. The addition of chiral centres (menthol) to the planar chirality of the ferrocenyl moiety led to a selectivity improvement, but we cannot exclude that this is a simple steric crowding effect. The 37% ee obtained at 40 °C with **7c** is, to our knowledge, one of the best results obtained with a (P,O) ferrocenyl ligand.[30–32,35,36]

3.3. Conclusion

Since the pioneering work by Cammidge and Buchwald on enantiomeric Suzuki–Miyaura coupling, many contributions on chiral ligand design have appeared but no ligand really emerges as universal. Despite the high

Table 3. Asymmetric Suzuki–Miyaura reaction between 1-bromo-2-methylnaphthalene and naphthylboronic acids using P-O ligands.[a]

Entry	Ligand	R^1	R^2	T (°C)	Reaction time (h)	Conversion[b] (%)	% ee[c]	TOF (h)[d]
1	**7a**-rac	Me	H	40	24	89	-	245
2	**7a**-rac	Me	H	50	24	100	-	403
3	**7a**-rac	Me	H	60	24	100	-	474
4	**7b-**(R)	Me	H	40	24	81	10	223
5	**7b-**(R)	Me	H	50	24	88	11	376
6	**7b-**(R)	Me	H	60	24	100	12	430
7	**7c-**(R)	Me	H	40	24	75	37	125
8	**7c-**(R)	Me	H	50	24	87	27	289
9	**7c-**(R)	Me	H	60	24	99	26	338

[a] Reagents and conditions: 1-bromo-2-methylnaphthalene (1.0 equiv), 1-naphthaleneboronic acid (1.2 equiv), $Pd_2(dba)_3$ (1.1 mol %), ligands **7a**–**c** (1.2 mol %), Cs_2CO_3 (2.3 equiv), toluene. [b] Determined by integration of characteristic ^1H NMR signals in the crude mixture. [c] Determined by HPLC with a Chiracel-OJ column. [d] evaluation after 10 min reaction.

steric hindrance of both substrates and reagents, the use of sterically hindered ligands (binaphthyl phosphines, ferrocenyl phosphines, etc., or more recently NHCs), which can stabilise very reactive 14e- palladium species, has led to increased catalytic activity, allowing running reactions under relatively mild conditions. However, increasing the steric crowding at the metal centre may also reduce the reagent's accessibility to the metal, thus decreasing the reaction rate. Indeed P,O ferrocenyl ligands (**7a**–**c**), which may be considered hemilabile ligands, gave higher catalytic activity than the strongly coordinating P,NHC bidentate ligands.

A literature survey shows that the best selectivities are generally obtained with reagents and substrates bearing polar moieties (phosphonates, amides, or aldehydes) at the *ortho* position relative to the reactive groups (halide or boronic acid), which is not observed with our phosphine-carbene ligands. Another observation to be made is that P,NHC ligands gave slightly higher ee's compared to P,O ferrocenyl ligands. This may be consistent with the hypothesis that bidendate ligand coordination (more strongly favoured for P,NHC ligands) leads to better chirality transfer. However, the role of the substituents and the ligands in enantioselectivity control is far from being fully understood, underlying the remaining challenges for the near future.

4. Rhodium(III) complex with a NHC-phosphine ligand for the direct functionalisation of C(sp^2)-H bonds

The direct C–H functionalisation of aryl substrates has emerged in the last 10 years as a very powerful synthetic methodology and a good alternative to more classical C–C coupling reactions, as it avoids the preparation of halogenated substrates and Grignard reagents or boronic acids, such as those involved in the KTC or Suzuki–Miyaura reactions, respectively. Although very important advances have been made using palladium-based catalysts,[45–50] rhodium also proved a valuable option as the simple Rh^{III} salt $[RhCp^*Cl_2]_2$ is capable of activating aromatic C(sp^2)-H bonds. Since the pioneering work by Fagnou,[51] Satoh and Miura,[52] and Jones,[53] many reviews have related the most important aspects of these reactions.[54–56] One limitation of this type of reaction, however, is the very poor variety of rhodium(III) catalysts reported. Apart from the ubiquitous $[RhCp^*Cl_2]_2$ and $[RhCp^*(MeCN)_3][X]_2$ complexes, the few others are also based on the Cp ligand,[57–62] the functionalisation of which is not trivial. This could be explained by the difficulty in finding rhodium(III)

complexes that possess three available coordination sites, which are necessary for the functionalisation of C–H bonds. There is therefore a need for new catalysts in this domain.

We have recently described an original strategy to access a new rhodium(III) complex by simple oxidation of rhodium(I) complexes bearing a redox-active ferrocenyl NHC-phosphine ligand (Figure 8).[63,64] The reaction is initiated by ferrocene oxidation, either by thianthrenium tetrafluoroborate (for complex **10**) or $AgBF_4$ (for complex **11**). In the presence of acetonitrile as solvent and as coordinating ligand, the oxidation products rearrange to give an intermediate tricationic rhodium(III) complex (observed spectroscopically) in which the ferrocene is back in its reduced state. The rhodium centre in this intermediate is very electrophilic and inserts into a ferrocene C–H bond to give the stable dicationic rhodium(III) complex **12**. The structure of this new, air-stable complex appeared very interesting to us as it is isoelectronic to the well-known $[RhCp^*(MeCN)_3][BF_4]_2$, which is commonly used as catalyst in C–H functionalisation reactions, and possesses three available coordination sites. It also stands out since it is not based on the Cp motif and, though obtained in a racemic form, possesses planar chirality. This prompted us to evaluate its performances in the Grignard-type arylation of 4-nitrobenzaldehyde via the C–H activation of 2-phenylpyridine (Figure 9).[65] Preliminary catalytic tests showed 33% conversion into the expected alcohol after 24 h at 65 °C in THF (^{1}H NMR measurement, nonoptimised conditions). The reaction was also carried out in 1,2-dichloroethane at 60 °C and gave 24% conversion after 24 h.

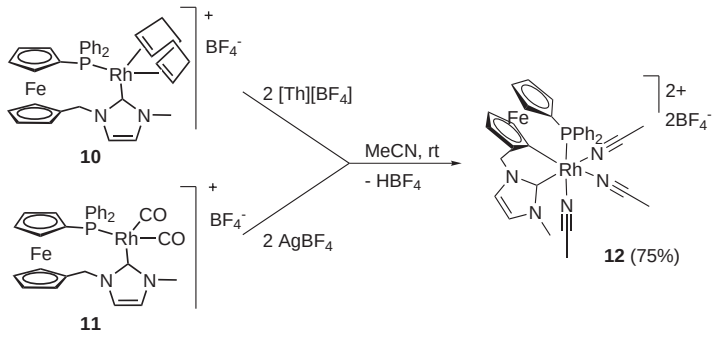

Figure 8. Synthesis of rhodium(III) complex **12** from rhodium(I) complexes **10** or **11**.

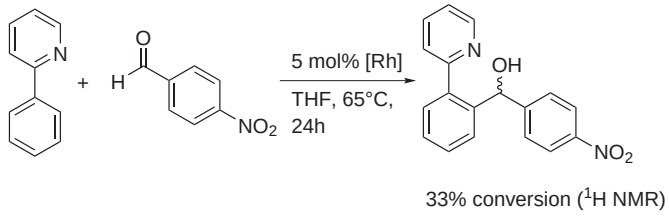

Figure 9. Grignard-type arylation of 4-nitrobenzaldehyde catalysed by Rh^{III} complex **12**.

One of the main challenges associated with the emerging asymmetric C–H functionalisation reaction is the development of adapted chiral ligands; therefore our future efforts will be devoted to the synthesis and optimisation of our rhodium(III) complexes, possibly in enantiopure form, in order to find the best possible C–H functionalisation catalyst.

5. Conclusion

We have reported here some recent results obtained in C–C coupling catalysis (Kumada–Tamao–Corriu, asymmetric Suzuki–Miyaura, C–H activation) using nonchiral P,NHC or chiral P,O and P,NHC ferrocenyl ligands synthesised by our group. These preliminary studies allowed us to achieve good catalytic activities albeit with only moderate enantiomeric excesses (up to 46% in the asymmetric Suzuki–Miyaura cross-coupling reaction using P,NHC ferrocenyl ligands). Future work will aim at designing new NHC, ferrocenyl phosphines or NHC ferrocenyl ligands, to improve both catalytic activity and enantioselectivity, and to better understand the relationships between ligands' structure and activity and selectivity, especially enantioselectivity in C–C coupling reactions through experimental and computational work, as we already started to carry out for other reactions.[66,67]

References

1. Magano, J.; Dunets, J. R. *Chem. Rev.* **2011**, *111*, 2177–2250.
2. Noël, T.; Buchwald, S. L. *Chem. Soc. Rev.* **2011**, *40*, 5010–5029.
3. Jana, R.; Pathak, T. P.; Sigma, M. S. *Chem. Rev.* **2011**, *111*, 1417–1492.
4. Han, F. S. *Chem. Soc. Rev.* **2013**, *42*, 5270–5298.
5. Routaboul, L.; Vincendeau, S.; Daran, J. C.; Manoury, E. *Tetrahedron: Asymmetry* **2005**, *16*, 2685–2690.
6. Mateus, N.; Routaboul, L.; Daran, J. C.; Manoury, E. *J. Organomet. Chem.* **2006**, *691*, 2297–2310.
7. Le Roux, E.; Malacea, R.; Manoury, E.; Poli, R.; Gonsalvi, L.; Peruzzini *Adv. Synth. Catal.* **2007**, *349*, 1064–1073.
8. Diab, L.; Gouygou, M.; Manoury, E.; Kalck, P.; Urrutigoïty, M. *Tetrahedron Lett.* **2008**, *49*, 5186–5189.
9. Biosca, M.; Coll, M.; Lagarde, F.; Brémond, E.; Routaboul, L.; Manoury, E.; Pàmies, O.; Poli, R.; Diéguez, M. *Tetrahedron* in press (doi: 10.1016/j.tet.2015.01.047).
10. Colacot, T. J. *Chem. Rev.* **2003**, *103*, 3101–3118.
11. Barbaro, P.; Bianchini, C.; Giambastini, G.; Parisel, S. L. *Coord. Chem. Rev.* **2004**, *248*, 2131–2150.
12. Manoury, E.; Poli, R. In *Catalysis by Metal Complexes (CMCO)*; Peruzzini, M.; Gonsalvi, L., Eds. Springer Verlag: Berlin, Germany, 2011, pp. 121–149.
13. Cesar, V.; Bellemin-Laponnaz, S.; Gade, L. H. *Chem. Soc. Rev.* **2004**, *33*, 619–636.
14. Wang, F.; Liu, L. J.; Wang, W.; Li, S.; Shi, M. *Coord. Chem. Rev.* **2012**, *256*, 804–853.
15. Zhang, D.; Wang, Q. *Coord. Chem. Rev.* **2015**, *286*, 1–16.
16. Wencel-Delord, J.; Panossian, A.; Leroux, F. R.; Colobert, F. *Chem. Soc. Rev.* **2015**, *44*, 3418–3430.
17. Loxq, P.; Manoury, E.; Poli, R.; Deydier, E.; Labande, A. *Coord. Chem. Rev.* in press (doi:10.1016/j.ccr.2015.07.006).
18. Kapdi, A. R. *Dalton Trans.* **2014**, *43*, 3021–3034.
19. Kumada, M. *Pure Appl. Chem.* **1980**, *52*, 669–679.
20. Herrmann, W. A. In *Applied Homogeneous Catalysis with Organometallic Compounds*; Cornils, B.; Herrmann, W. A., Eds. Wiley-VCH, Weinheim, Germany, 2002.
21. Herrmann, W. A.; Reisinger, C. P.; Spiegler, M. *J. Organomet. Chem.* **1998**, *557*, 93–96.
22. Weskamp, T.; Böhm, V. P. W.; Herrmann, W. A. *J. Organomet. Chem.* **1999**, *585*, 348–352.
23. Böhm, V. P. W.; Weskamp, T.; Gstöttmayr, C. W. K.; Herrmann, W. A. *Angew. Chem. Int. Ed.* **2000**, *39*, 1602–1604.
24. Wolf, J.; Labande, A.; Daran, J. C.; Poli, R. *J. Organomet. Chem.* **2006**, *691*, 433–443.
25. Wolf, J.; Labande, A.; Natella, M.; Daran, J. C.; Poli, R. *J. Mol. Catal. A: Chem.* **2006**, *259*, 205–212.

26. Henrion, M.; Ritleng, V.; Chetcuti, M. J. *ACS Catal.* **2015**, *5*, 1283–1302.
27. Tasker, S. Z.; Standley, E. A.; Jamison, T. F. *Nature* **2014**, *509*, 299–309.
28. Yin, J.; Buchwald, S.L. *J. Am. Chem. Soc.* **2000**, *122,* 12051–12052.
29. Shen, X.; Jones, G. O.; Watson, D. A.; Bhayana, B.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 11278–11287.
30. Cammidge, A. N.; Crépy, K. V. L. *Chem. Commun.* **2000**, 1723–1724.
31. Cammidge, A. N.; Crépy, K. V. *Tetrahedron* **2004**, *60*, 4377–4386.
32. Herrbach, A.; Marinetti, A; Baudoin, O.; Guénard, D.; Guéritte, F. *J. Org. Chem.* **2003**, *68*, 4897–4905.
33. Genov, M.; Almorín, A.; Espinet, P. *Tetrahedron: Asymmetry* **2007**, *18*, 625–627.
34. Genov, M.; Almorín, A.; Espinet, P. *Chem. Eur. J.* **2006**, *12*, 9346–9352.
35. Jensen, J. F.; Johannsen, M. *Org. Lett.* **2003**, *5*, 3025–3028.
36. Schaarschmidt, D.; Lang, H. *Eur. J. Inorg. Chem.* **2010**, 4811–4821.
37. Schaarschmidt, D.; Grumbt, M.; Hildbrandt, A.; Lang, H. *Eur. J. Org. Chem.* **2014**, 6676–6685.
38. Debono, N.; Labande, A.; Manoury, E.; Daran, J. C.; Poli, R. *Organometallics* **2010**, *29*, 1879–1882.
39. Loxq, P.; Debono, N.; Gülcemal, S.; Daran, J. C.; Manoury, E.; Poli, R.; Cetinkaya, B.; Labande, A. *New J. Chem.* **2014**, *38*, 338–347.
40. Bayda, S.; Cassen, A.; Daran, J. C.; Audin, C.; Poli, R.; Manoury, E.; Deydier, E. *J. Organomet. Chem* **2014**, *772-773*, 258–264.
41. Mateus, M.; Routaboul, L.; Daran, J. C.; Manoury, E. *J. Organomet. Chem.* **2006**, *691*, 2297–2310.
42. Yılmaz, Ü.; Küçükbay, H.; Türktekin Çelikesir, S.; Akkurt, M.; Büyükgüngör, O. *Turk. J. Chem.* **2013**, *37*, 721–733.
43. Küçükbay, H.; Şireci, N.; Yılmaz, Ü.; Deniz, S.; Akkurt, M.; Baktır, Z.; Büyükgüngör, O. *Turk. J. Chem.* **2012**, *36*, 201–217.
44. Yılmaz, U.; Küçükbay, H.; Sireci, N.; Akkurt, M.; Günal, S.; Durmaz, R.; Nawaz Tahir, M. *Appl. Organomet. Chem.* **2011**, *25*, 366–373.
45. Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215–1292.
46. Wencel-Delord, J.; Dröge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740–4761.
47. Baudoin, O. *Chem. Soc. Rev.* **2011**, *40*, 4902–4911.
48. Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147–1169.
49. Sun, C. L.; Li, B. J.; Shi, Z. J. *Chem. Commun.* **2010**, *46*, 677–685.
50. Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem. Int. Ed.* **2009**, *48*, 9792–9826.
51. Stuart, D. R.; Bertrand-Laperle, M.; Burgess, K. M. N.; Fagnou, K. *J. Am. Chem. Soc.* **2008**, *130*, 16474–16475.
52. Ueura, K.; Satoh, T.; Miura, M. *Org. Lett.* **2007**, *9*, 1407–1409.
53. Li, L.; Brennessel, W. W.; Jones, W. D. *J. Am. Chem. Soc.* **2008**, *130*, 12414–12419.
54. Kuhl, N.; Schröder, N.; Glorius, F. *Adv. Synth. Catal.* **2014**, *356*, 1443–1460.
55. Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651–3678.
56. Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814–825.
57. Hyster, T. K.; Rovis, T. *Chem. Sci.* **2011**, *2*, 1606–1610.
58. Hyster, T. K.; Knörr, L.; Ward, T. R.; Rovis, T. *Science* **2012**, *338*, 500–503.
59. Hyster, T. K.; Dalton, D. M.; Rovis, T. *Chem. Sci.* **2015**, *6*, 254–258.
60. Davis, T. A.; Wang, C.; Rovis, T. *Synlett* **2015**, *26*, 1520–1524.
61. Ye, B.; Cramer, N. *Acc. Chem. Res.* **2015**, *48*, 1308–1318 and references therein.

62. Ye, B.; Cramer, N. *Synlett* **2015**, *26*, 1490–1495.

63. Labande, A.; Debono, N.; Sournia-Saquet, A.; Daran, J. C.; Poli, R. *Dalton Trans.* **2013**, *42*, 6531–6537.

64. Debono, N.; Daran, J. C.; Poli, R.; Labande, A. *Polyhedron* **2015**, *86*, 57–63.

65. Yang, L.; Correia, C. A.; Li, C. J. *Adv. Synth. Catal.* **2011**, *353*, 1269–1273.

66. Wei, M. M.; García-Melchor, M.; Lledós, A.; Audin, C.; Daran, J. C.; Poli, R.; Deydier, E.; Manoury, E. *Organometallics* **2012**, *31*, 6669–6680.

67. Hayes, J. M.; Deydier, E.; Ujaque, G.; Lledós, A.; Malacea, R.; Manoury, E.; Vincendeau, S.; Poli, R. *ACS Catal.* **2015**, *5*, 4368–4376.