the 3′-overhang for state **1′** is fully complementary to its loop, whereas the 5′-overhang for **1″** is complementary to only two of the four bases, thus possibly providing a facile route to **1″** and a faster rate constant in the forward direction.

[11] a) M. E. Burkard, D. H. Turner, I. Tinoco, Jr. in *The RNA World*, *Second Edition* (Eds.: R. F. Gesteland, T. R. Cech, J. F. Atkins), CSHL Press, New York, **1999**, pp. 675 – 680; V. P. Antao, S. Y. Lai, I. Tinoco, Jr., *Nucleic Acids Res.* **1991**, *19*, 5901 – 5905; c) R. Kirchner, M. Vogtherr, S. Limmer, M. Sprinzl, *Antisense Nucleic Acid Drug Dev.* **1998**, *8*, 507 – 516.

[12] For a thermodynamic comparison of nucleotide loop replacements with non-nucleotide linkers, see: W.Pils, R. Micura, *Nucleic Acids Res.* **2000**, *28*, 1859 – 1863.

[13] For an impressive example of an RNA sequence that can adopt two different conformations and thereby exert different catalytic activities, see: a) E. A. Schultes, D. P. Bartel, *Science* **2000**, 448 – 452; for further examples of stable alternative RNA conformers, see: *Tetrahymena* ribozyme: b) J. Pan, D. Thirumalai, S. A. Woodson, *J. Mol. Biol.* **1997**, *273*, 7 – 13; c) D. K. Treiber, M. S. Rock, P. P. Zarrinkar, J. R. Williamson, *Science* **1998**, *279*, 1943 – 1946; hepatitis delta virus (HDV) ribozyme: d) A. T. Perrotta, M. D. Been, *J. Mol. Biol.* **1998**, *279*, 361 – 373; tRNA: e) E. Madone, C. Florentz, R. Giegé, J. Lapointe, *Nucleic Acids Res.* **1999**, *27*, 3583 – 3588; f) V. Serebrov, R. J. Clarke, H. J. Gross, L. Kisselev, *Biochemistry* **2001**, *40*, 6688 – 6698; HIV-1 leader RNA: H. Huthoff, B. Berkhout, *Nucleic Acids Res.* **2001**, *29*, 2594 – 2600; RNA Phage MS2: D. van Meerten, G. Girard, J. van Duin, *RNA* **2001**, *7*, 483 – 494; g) J. Flinders, T. Dieckmann, *J. Mol. Biol.* **2001**, *308*, 665 – 679.

[14] a) M. Wu, I. Tinoco, Jr., *Proc. Natl. Acad. Sci. USA* **1998**, *95*, 11555 – 11560; b) K. A. LeCuyer, D. M. Crothers, *Proc. Natl. Acad. Sci. USA* **1994**, *91*, 3373 – 3377; c) T. C. Gluick. R. B. Gerstner, D. E. Draper, *J. Mol. Biol.* **1997**, *270*, 451 – 463.

[15] For computer-simulated RNA equilibria, see: a) C. Flamm, I. L. Hofacker, S. Maurer-Stroh, P. F. Stadler, M. Zehl, *RNA* **2001**, *7*, 254 – 265; b) S. Wuchty, W. Fontana, I. L. Hofacker, P. Schuster, *Biopolymers* **1999**, *49*, 145 – 165.

[16] a) P. Brion, E. Westhof, *Annu. Rev. Biophys. Biomol. Struct.* **1997**, *26*, 113 – 137; b) I. Tinoco, Jr., C. Bustamante, *J. Mol. Biol.* **1999**, *293*, 271 – 281.

[17] For an example of an rRNA databank, see: Y. Van de Peer, P. Rijk, J. Winkelmans, R. De Wachter, *Nucleic Acids Res.* **2000**, *28*, 175 – 176.

[18] It has been reported that mutations of the rRNA dimethylase ksgAp of *E. coli* block the $m^6{}_2Am^6{}_2A$ dimethylation of 16S rRNA; however, they do not interfere with rRNA processing. Consequently, the mutants synthesize the SSU of rRNA in which helix 45 is not modified. These allow the growth of the mutant strains at a reduced rate. The unmodified ribosomes are defective in several aspects of translation in vitro; see: a) P. H. van Knippenberg in *Structure, Function, and Genetics of Ribosomes* (Eds.: B. Hardesty, G. Kramer), Springer, New York, NY, **1986**, pp. 412 – 424; b) D. Nègre, C. Weizmann, J. Ofengand, *Proc. Natl. Acad. Sci. USA* **1989**, *86*, 4902 – 4906; c) D. L. J. Lafontaine, D. Tollervey in *Modification and Editing of RNA* (Eds.: H. Grosjean, R. Benne), ASM, Washington, DC, **1998**, pp. 281 – 288.

Iron-Catalyzed Cross-Coupling Reactions of Alkyl-Grignard Reagents with Aryl Chlorides, Tosylates, and Triflates**

Alois Fürstner* and Andreas Leitner

Classical cross-coupling processes such as the Kumada – Corriu, Negishi, Stille, or Suzuki reaction are of utmost importance for modern organic synthesis.[1] These transformations are usually catalyzed by palladium or nickel complexes, although no inherent restriction to these late transition metals exists. Aryl iodides and bromides are the best substrates; only recently have special ligands been designed that allow the scope of these methods to be extended to aryl chlorides.[2] Aryl triflates represent yet another class of suitable starting materials, whereas less expensive sulfonates have hardly been used so far because of their lack of activity in most cases.[3]

Herein we describe initial studies on the development of an alternative cross-coupling procedure which allows the attachment of alkyl groups to arenes in a very efficient way.[4] This method is distinguished by a number of notable advantages:

1) expensive nobel metal catalysts are replaced by cheap, stable, commercially available and toxicologically benign iron salts
2) aryl chlorides and triflates provide a priori better results than the corresponding bromides or iodides
3) aryl tosylates turned out to be suitable starting materials as well
4) the reaction is performed under "ligand-free" conditons
5) the reaction times are usually very short.

Although iron salts were proposed as catalysts for cross-coupling reactions by Kochi et al. as early as 1971,[5] they attracted little attention in the following decades.[6] Their scope remained essentially limited to reactions of Grignard reagents with *alkenyl* halides.[6, 7] Successful applications to other types of substrates, in particular to *aryl* halides, have not been reported. Moreover, the mechanism of the iron-catalyzed reactions remained rather obscure, whereas detailed insights into most of the prominent palladium-catalyzed processes have been gained over the years.[1] It has been proposed that Fe^0 or Fe^I species constitute the catalytically relevant intermediates,[5] although no secured information as to their structure or mode of action could be obtained. Alternatively, "super-ate" complexes of Fe^{II} have been suggested as the active species.[8]

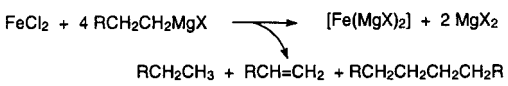
Taking recent advancements in the field of "inorganic Grignard reagents" into consideration,[9] however, these hypotheses seem to be highly unlikely and called for a re-evaluation of iron-catalyzed cross-coupling chemistry. It is now well established that $FeCl_2$ reacts with *four* equivalents of

[*] Prof. Dr. A. Fürstner, Dipl.-Ing. A. Leitner
Max-Planck-Institut für Kohlenforschung
45470 Mülheim an der Ruhr (Germany)
Fax: (+49) 208-306-2994
E-mail: fuerstner@mpi-muelheim.mpg.de

[**] This work was supported by the Deutsche Forschungsgemeinschaft (Leibniz program) and the Fonds der Chemischen Industrie. We thank Prof. B. Bogdanović for helpful discussions.

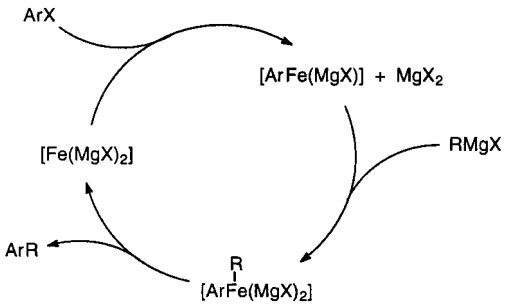
  1433-7851/02/4104-0609 $ 17.50+.50/0

RMgX to give a new species of the formal composition $[Fe(MgX)_2]$.[10] This implies that the reduction process does not stop once a zerovalent iron species "Fe^0" is formed, but rather generates Fe^{-II} centers (Scheme 1),[9, 11] which are



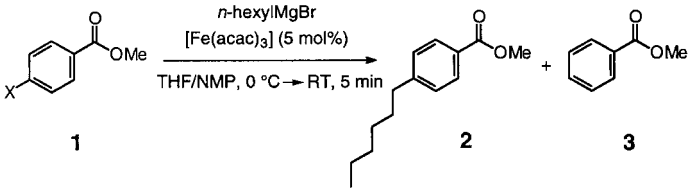
Scheme 1. Known stoichiometry for the formation of an inorganic Grignard reagent of iron.[9, 11]

capable of oxidatively inserting into aryl halides due to their highly nucleophilic character.[11, 12] We anticipated that the ensuing Fe^0 complexes might again be alkylated by a suitable Grignard reagent.[13] Subsequent reductive coupling should then form the desired product and regenerate the catalytically active $[Fe(MgX)_2]$ species (Scheme 2).[10, 14]



Scheme 2. Proposed formal catalytic cycle for the iron-catalyzed cross-coupling process.[14]

Initial attempts to verify this concept using aryl iodide **1a** (X = I; Scheme 3) or aryl bromide **1b** (X = Br) were only partly successful. Although we were able to detect the cross-coupling product **2** in the reaction mixture, the reduction of the substrates with formation of compound **3** prevailed (Table 1). In marked contrast, however, the use of chloride **1c** as the starting material led to the almost quantitative formation of the desired alkylbenzoic acid ester **2**; notably, the



Scheme 3. Optimization of the iron-catalyzed cross-coupling reaction of substrate **1**, (see Table 1). NMP = *N*-methylpyrrolidone.

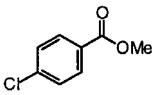
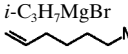
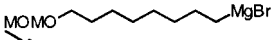
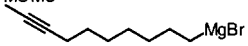
Table 1. Screening of different substrates in the iron catalyzed cross coupling reaction depicted in Scheme 3.

Entry	X	Yield [GC, %]	
		2	**3**
1	I	27	46
2	Br	38	50
3	Cl	> 95	–
4	OTf	> 95	–
5	OTs	> 95	–

conversion is quantitative after a reaction time of less than 5 minutes, and no competing attack of the Grignard reagent on the methyl ester function of the substrate **1c** has been observed.[15] It turned out that the corresponding triflate **1d** (X = OTf) and even the tosylate **1e** (X = OTs) perform equally well, providing product **2** in excellent yields and high reaction rates.

The reaction is virtually independent of the chosen iron salt (Table 2, entries 1–4, 7–9).[5, 6] The cheap and non-hygroscopic $[Fe(acac)_3]$ is the most convenient precatalyst from the practical point of view. Only for secondary alkyl Grignard reagents the use of [Fe(salen)Cl] is recommended (Table 2, entry 9). The method, however, was found to be highly responsive to the chosen nucleophile. In addition to *n*-alkyl– and *sec*-alkylmagnesium halides with ≥ 2 carbon atoms, which uniformly react without incident, trialkylzincates also constitute suitable reagents (Table 2, entry 16). The use of an organolithium compound, however, failed to afford any cross-coupling product (Table 2, entry 17). We tentatively ascribe

Table 2. Screening of the performance of different iron salts and nucleophiles in cross-coupling reactions with two different aryl chlorides.[a]

Entry	ArCl	RM	Fe salt [5 %]	ArR [%][b]
1		*n*-$C_6H_{13}MgBr$	$[Fe(acac)_2]$	90
2		*n*-$C_6H_{13}MgBr$	$[Fe(acac)_3]$	91
3		*n*-$C_6H_{13}MgBr$	$FeCl_3$	88
4		*n*-$C_6H_{13}MgBr$	[Fe(salen)Cl]	96
5		C_2H_5MgBr	$[Fe(acac)_3]$	> 95
6		*n*-$C_6H_{13}MgBr$	$[Fe(acac)_3]$	> 95
7		*n*-$C_6H_{13}MgBr$	$FeCl_2$	> 95
8		*n*-$C_{14}H_{29}MgBr$	$[Fe(acac)_3]$	> 95
9		*i*-C_3H_7MgBr	[Fe(salen)Cl]	59
10			$[Fe(acac)_3]$	91[c]
11			$[Fe(acac)_3]$	88[c]
12			$[Fe(acac)_3]$	85[c]
13		$H_2C{=}CHMgBr$	$[Fe(acac)_3]$	0
14		$H_2C{=}CHCH_2MgBr$	$[Fe(acac)_3]$	0
15		C_6H_5MgBr	$[Fe(acac)_3]$	28
16		$Et_3ZnMgBr$	$[Fe(acac)_3]$	93
17		*n*-C_4H_9Li	$[Fe(acac)_3]$	0

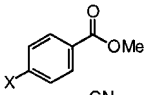
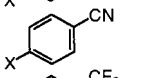
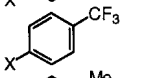
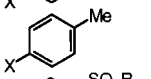
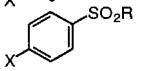
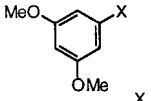
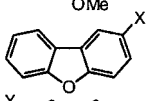
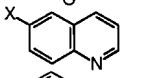
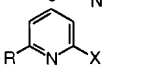
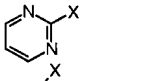
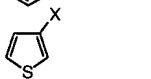
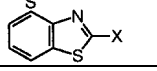
[a] acac = acetylacetonato, salen = *N*,*N*-ethylenebis(salicylidenamidato), MOM = methoxymethyl. [b] GC yields unless stated otherwise. [c] Yield of isolated product.

this distinct behavior to the need to form a rather covalent Fe–M (M = Mg, Zn) bond in the active species.[9, 11, 16] In stark contrast to the successful use of alkylmagnesium halides, all aryl-, allyl- and alkenyl-Grignard reagents investigated invariably led to poor results (Table 2, entries 13–15). This might be caused by a competing catalytic decomposition of such organometallic species in the presence of transition metal salts and aryl halides to form biaryls or dienes, respectively, as documented in a series of classical publications of Kharasch et al.[17]

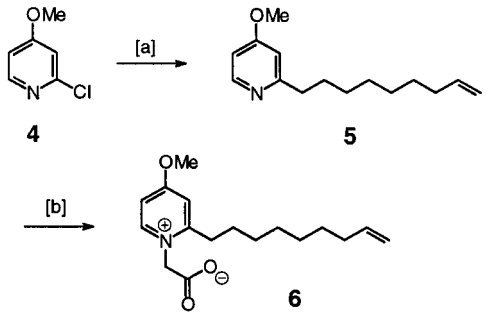
With regard to the substrate scope, the iron-catalyzed process turned out to be widely applicable. As can be seen from the results compiled in Table 3, all moderately electron-

  1433-7851/02/4104-0610 $ 17.50+.50/0

Table 3. Yields [%] of iron-catalyzed cross-coupling reactions of alkyl-Grignard reagents with aryl chlorides, triflates, and tosylates.

Nr.	ArX	RMgX	X = Cl	X = OTf	X = OTs
1		*n*-C_6H_{13}MgBr	91	87	83
2		*n*-C_6H_{13}MgBr	91	80	74
3		*n*-$C_{14}H_{29}$MgBr	94	72	75
4		*n*-$C_{14}H_{29}$MgBr	0	81	0
5		*n*-C_6H_{13}MgBr	85 (R = O*i*Pr)		
6			94 (R = N*i*Pr_2)		
7		*n*-$C_{14}H_{29}$MgBr	0	90	0
8		*n*-$C_{14}H_{29}$MgBr		81	
9		*n*-$C_{14}H_{29}$MgBr	92	74	82
10		*n*-$C_{14}H_{29}$MgBr	81 (R = H)		
11			95 (R = OMe)		
12		*n*-$C_{14}H_{29}$MgBr	93		
13		*n*-$C_{14}H_{29}$MgBr	41		
14		*n*-$C_{14}H_{29}$MgBr	68		

deficient aryl chlorides and tosylates investigated react with good to excellent yields. In the case of electron-rich arenes, however, the use of aryl triflates is necessary (Table 3, entries 4, 7, 8). In this way a host of different carbo- and heterocyclic products can be prepared. Of particular note among them are the long-chain alkylbenzene sulfonate shown in entry 5 of Table 3, which serves as a precursor for a biologically degradable detergent,[18] as well as compound **5** (Scheme 4) as the key intermediate of a synthesis of the cytotoxic marine natural product montipyridine **6**.[19] The fact that this new method allows the attachment of unsaturated side chains to arene rings (Table 2 and Scheme 4) complements existing methodology for the preparation of substrates suitable for our studies into alkene and alkyne metathesis.[20, 21]



Scheme 4. Synthesis of the cytotoxic natural product montipyridine **6**. [a] 8-Nonenylmagnesium bromide, [Fe(acac)$_3$] (5 mol%), THF/NMP, 0 °C → RT, 81%; [b] 1. $BrCH_2COO(tBu)$, 40 °C; 2. F_3CCOOH, Et_3SiH, CH_2Cl_2, 74%.

The assumed mechanistic scenario outlined above is substantiated by the following control experiments. Thus, it has been shown that even highly activated $Fe^{0(*)}$ powder[22] does not readily insert into the C–Cl bond of substrate **1c** even at elevated temperatures. If, however, a suspension of $Fe^{0(*)}$ is stirred in the presence of an excess of *n*-$C_{14}H_{29}$MgCl, the slow dissolution of the solid material with formation of a dark brown to black, homogeneous solution is observed. The latter is able to efficiently catalyze the cross-coupling of added **1c** with the Grignard reagent. This finding is in line with the notion that Fe^0 centers can be alkylated by organomagnesium compounds and thereby get reduced to Fe species with formally negative oxidation states (e.g. [Fe(MgX)$_2$])[10] which likely account for the observed catalytic turnover.[13] Ongoing studies are aimed at corroborating these mechanistic assumptions, at improving the results in the cross-coupling of arylmagnesium halides with chloroarenes, and at implementing this novel methodology into natural product synthesis.

Experimental Section

A flame-dried two-necked flask was charged under argon with methyl 4-chlorobenzoate (**1c**; 1.00 g, 5.86 mmol), [Fe(acac)$_3$] (103 mg, 0.29 mmol), THF (35 mL), and NMP (3.3 mL). A solution of *n*-hexylmagnesium bromide (2 M in Et_2O, 3.5 mL, 7.00 mmol) was added by syringe to the resulting red solution, causing an immediate color change to dark brown and finally to violet. The resulting mixture was stirred for 5–10 min, the reaction was diluted with Et_2O and was carefully quenched upon addition of aqueous HCl (1 M, ca. 10 mL). Standard extractive work-up followed by flash chromatography of the crude product (hexanes/ethyl acetate, 30/1) provided compound **2** as a colorless syrup (1.24 g, 91%). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.90$ (d, $J = 8.3$ Hz, 2H), 7.19 (d, $J = 8.4$ Hz, 2H), 3.84 (s, 3H), 2.59 (t, $J = 7.7$ Hz, 2H), 1.57 (m, 2H), 1.21–1.29 (m, 6H), 0.84 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 167.1$, 148.4, 129.2, 128.7, 51.8, 35.9, 31.2, 31.0, 28.9, 22.5, 13.9; IR: $\tilde{\nu} = 1724$ cm^{-1}; MS (EI): *m*/*z* (rel. intensity): 220 (50, [M^+]), 189 (39), 150 (100), 91 (54), 43 (17).

Received: October 12, 2001 [Z 18053]

[1] *Metal-catalyzed Cross-coupling Reactions* (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, **1998**.

[2] For recent developments see: a) C. Dai, G. C. Fu, *J. Am. Chem. Soc.* **2001**, *123*, 2719–2724; b) D. W. Old, J. P. Wolfe, S. L. Buchwald, *J. Am. Chem. Soc.* **1998**, *120*, 9722–9723; c) J. Huang, S. P. Nolan, *J. Am. Chem. Soc.* **1999**, *121*, 9889–9890; d) B. H. Lipshutz, *Adv. Synth. Catal.* **2001**, *343*, 313–326; e) A. Fürstner, A. Leitner, *Synlett* **2001**, 290–292; f) A. Zapf, A. Ehrentraut, M. Beller, *Angew. Chem.* **2000**, *112*, 4315–4317; *Angew. Chem. Int. Ed.* **2000**, *39*, 4153–4155; g) V. P. W. Böhm, C. W. K. Gstöttmayr, T. Weskamp, W. A. Herrmann, *J. Organomet. Chem.* **2000**, *595*, 186–190; h) X. Bei, H. W. Turner, W. H. Weinberg, A. S. Guram, J. L. Petersen, *J. Org. Chem.* **1999**, *64*, 6797–6803; i) J. P. Wolfe, R. A. Singer, B. H. Yang, S. L. Buchwald, *J. Am. Chem. Soc.* **1999**, *121*, 9550–9561; j) A. F. Indolese, *Tetrahedron Lett.* **1997**, *38*, 3513–3516; k) S. Saito, S. Oh-tani, N. Miyaura, *J. Org. Chem.* **1997**, *62*, 8024–8030; l) A. F. Littke, C. Dai, G. C. Fu, *J. Am. Chem. Soc.* **2000**, *122*, 4020–4028; m) M. T. Reetz, R. Breinbauer, K. Wanninger, *Tetrahedron Lett.* **1996**, *37*, 4499–4502; n) R. Stürmer, *Angew. Chem.* **1999**, 3509–3510; *Angew. Chem. Int. Ed.* **1999**, *38*, 3307–3308; o) for a recent paper describing catalyzed alkyl–alkyl cross-coupling reactions see: M. R. Netherton, C. Dai, K. Neuschütz, G. C. Fu, *J. Am. Chem. Soc.* **2001**, *123*, 10099–10100.

[3] For the activation of aryl mesylates and tosylates by Ni^0 catalysts see: a) V. Percec, J.-Y. Bae, D. H. Hill, *J. Org. Chem*. **1995**, *60*, 1060 – 1065; b) Y. Kobayashi, R. Mizojiri, *Tetrahedron Lett*. **1996**, *37*, 8531 – 8534; c) D. Zim, V. R. Lando, J. Dupont, A. L. Monteiro, *Org. Lett*. **2001**, *3*, 3049 – 3051.

[4] a) The importance of aryl – alkyl cross-coupling is evident from the following review: S. J. Danishefsky, S. R. Chemler, D. Trauner, *Angew. Chem*. **2001**, *113*, 4676 – 4701; *Angew. Chem. Int. Ed.* **2001**, *40*, 4544 – 4568; for pertinent examples from our group see: b) A. Fürstner, I. Konetzki, *J. Org. Chem*. **1998**, *63*, 3072 – 3080; c) A. Fürstner, I. Konetzki, *Tetrahedron* **1996**, *52*, 15071 – 15078; d) A. Fürstner, G. Seidel, *J. Org. Chem*. **1997**, *62*, 2332 – 2336.

[5] a) M. Tamura, J. Kochi, *J. Am. Chem. Soc*. **1971**, *93*, 1487 – 1489; b) S. M. Neumann, J. K. Kochi, *J. Org. Chem*. **1975**, *40*, 599 – 606; c) R. S. Smith, J. K. Kochi, *J. Org. Chem*. **1976**, *41*, 502 – 509; d) J. K. Kochi, *Acc. Chem. Res*. **1974**, *7*, 351 – 360.

[6] a) G. Cahiez, H. Avedissian, *Synthesis* **1998**, 1199 – 1205; b) G. A. Molander, B. J. Rahn, D. C. Shubert, S. E. Bonde, *Tetrahedron Lett*. **1983**, *24*, 5449 – 5452; c) C. K. Reddy, P. Knochel, *Angew. Chem*. **1996**, *108*, 1812 – 1813; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1700 – 1701; d) A. Fürstner, H. Brunner, *Tetrahedron Lett*. **1996**, *37*, 7009 – 7012; e) M. A. Fakhakh, X. Franck, R. Hocquemiller, B. Figadère, *J. Organomet. Chem*. **2001**, *624*, 131 – 135.

[7] Vinylsulfones undergo similar reactions: J.-L. Fabre, M. Julia, J.-N. Verpeaux, *Tetrahedron Lett*. **1982**, *23*, 2469 – 2472.

[8] T. Kauffmann, *Angew. Chem*. **1996**, *108*, 401 – 418; *Angew. Chem. Int. Ed. Engl*. **1996**, *35*, 386 – 403, and literature cited therein.

[9] a) L. E. Aleandri, B. Bogdanović in *Active Metals: Preparation, Characterization, Applications* (Ed.: A. Fürstner), VCH, Weinheim, **1996**, pp. 299 – 338; b) L. E. Aleandri, B. Bogdanović, P. Bons, C. Dürr, A. Gaidies, T. Hartwig, S. C. Huckett, M. Lagarden, U. Wilczok, R. A. Brand, *Chem. Mater*. **1995**, *7*, 1153 – 1170.

[10] EXAFS analyses indicate that $[Fe(MgX)_2]$ likely exists in form of small clusters of this net stoichiometry, cf. refs. [9, 11].

[11] B. Bogdanović, M. Schwickardi, *Angew. Chem*. **2000**, *112*, 4788 – 4790; *Angew. Chem. Int. Ed.* **2000**, *39*, 4610 – 4612.

[12] G. Siedlaczek, M. Schwickardi, U. Kolb, B. Bogdanović, D. G. Blackmond, *Catal. Lett*. **1998**, *55*, 67 – 72.

[13] Formally speaking, this corresponds to one of the elementary steps that has to be passed through during the formation of $[Fe(MgX)_2]$ from $FeCl_2$ and RMgX.

[14] It is explicitly pointed out that all intermediates depicted in the catalytic cycle are solely meant as a *formal* representation of the reactive species but do not imply any structural information whatsoever.

[15] If the reduction of the aryl halides **1a** – **c** leading to the formation of **3** occurs via a radical pathway, the higher energy of the σ* orbital of the C–Cl bond as compared to that of a C–I or C–Br bond might explain the observed selectivities.

[16] The strongly covalent character of a Fe–Mg bond is evident from studies on well defined intermetallic complexes such as [Cp(dppe)-Fe–MgBr] (dppe = 1,2-(diphenylphosphanyl)ethane): a) H. Felkin, P. J. Knowles, B. Meunier, A. Mitschler, L. Ricard, R. Weiss, *J. Chem. Soc. Chem. Commun*. **1974**, 44; b) H. Felkin, P. J. Knowles, B. Meunier, *J. Organomet. Chem*. **1978**, *146*, 151 – 167; c) G. B. McVicker, *Inorg. Chem*. **1975**, *14*, 2087 – 2092.

[17] a) M. S. Kharasch, E. K. Fields, *J. Am. Chem. Soc*. **1941**, *63*, 2316 – 2320; b) M. S. Kharasch, W. Nudenberg, S. Archer, *J. Am. Chem. Soc*. **1943**, *65*, 495 – 498.

[18] K. Kosswig in *Ullmann's Encyclopedia of Industrial Chemistry*, *Vol. A25*, VCH, Weinheim, **1994**, pp. 747 – 817.

[19] N. Alam, J. Hong, C. O. Lee, K. S. Im, B. W. Son, J. S. Choi, W. C. Choi, J. H. Jung, *J. Nat. Prod*. **2001**, *64*, 956 – 957.

[20] A. Fürstner, *Angew. Chem*. **2000**, *112*, 3140 – 3172; *Angew. Chem. Int. Ed.* **2000**, *39*, 3012 – 3043.

[21] A. Fürstner, C. Mathes, C. W. Lehmann, *Chem. Eur. J.* **2001**, *7*, 5299 – 5317, and references therein.

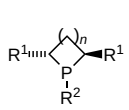
[22] a) A. V. Kavaliunas, A. Taylor, R. D. Rieke, *Organometallics* **1983**, *2*, 377 – 383; b) A. Fürstner, *Angew. Chem.* **1993**, *105*, 171 – 197; *Angew. Chem. Int. Ed. Engl*. **1993**, *32*, 164 – 189.

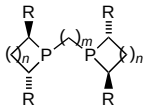
Mono- and Bidentate Phosphinanes—New Chiral Ligands and Their Application in Catalytic Asymmetric Hydrogenations**

Markus Ostermeier, Jan Prieß, and Günter Helmchen*

Dedicated to Professor Dieter Hoppe on the occasion of his 60th birthday

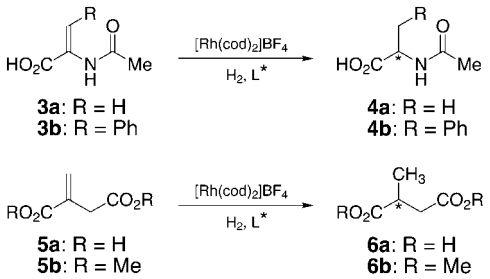
Chiral phosphanes possessing a modular make-up are important as ligands for asymmetric catalysis with transition metal complexes. The ethylene-bridged BPE ligands **2** and the 1,2-phenylene-bridged DuPHOS ligands,[1] introduced by Burk et al., and analogues[2] belong to the most effective ligands and were found to be particularly successful in enantioselective hydrogenations. Even with the monodentate phosphanes **1a** and **1b** enantiomeric excesses of up to 84 and 82 % *ee,* respectively, were achieved in the hydrogenation of





1a: n = 1; R^1 = CH_3, R^2 = Ph **2a**: m = n = 2; R = Me
1b: n = 2; R^1 = Ph, R^2 = Ph **2b**: m = n = 2; R = Et

acetamidocinnamic acid (**3a**) (Scheme 1); however, only 12 % *ee* were obtained with **1a** in the case of substrate **5b**.[3, 4] With the chelate ligands **2a** and **2b** hydrogenations of methyl 2-acetamidoacrylate furnished 91 and 98 % *ee*, respectively.[1b]



Scheme 1. Asymmetric catalytic hydrogenations. cod = cycloocta-1,5-diene, L* = chiral ligand.

Upon inspection of the literature it was observed that phosphetanes[5] (**1**, $n = 1$) and phospholanes[1–4] (**1**, $n = 2$) had been studied intensively and phosphiranes[6] marginally, surprisingly however, analogous phosphinanes (**1**, $n = 3$) were found to be unknown. Since there is a marked influence of ring size on the properties of ligands, we decided to fill this void in the arsenal of ligands. We now report the first ligands

[*] Prof. Dr. G. Helmchen, Dipl.-Chem. M. Ostermeier, Dr. J. Prieß
Organisch-chemisches Institut, Universität Heidelberg
Im Neuenheimer Feld 270, 69120 Heidelberg (Germany)
Fax: (+49) 6221-54-4205
E-mail: G.Helmchen@urz.uni-heidelberg.de

[**] This work was supported by the Fonds der Chemischen Industrie (Kekulé scholarship for M. O.). We thank Dr. F. Rominger for the X-ray crystal structure analysis.

  1433-7851/02/4104-0612 $ 17.50+.50/0