Palladium-catalysed Enantioselective Grignard Cross Coupling with Use of a new Ferrocenylaminophosphine Ligand

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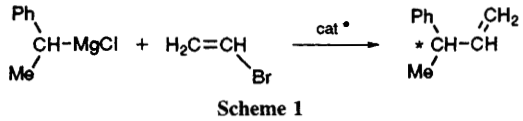
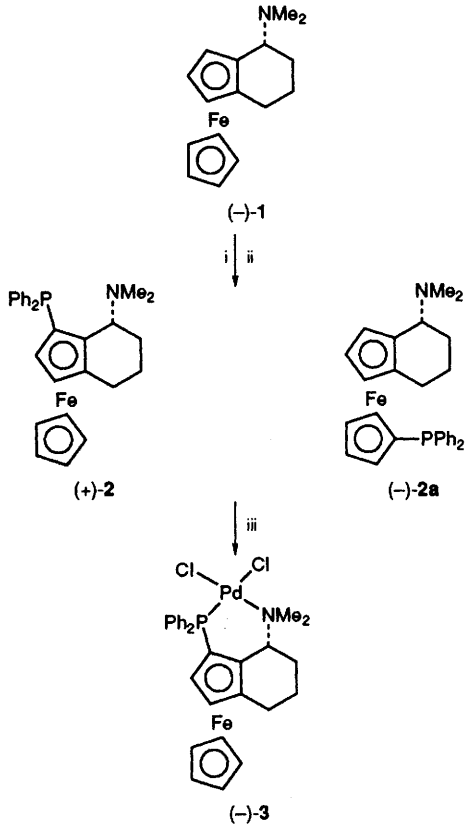
A new ferrocenylaminophosphine ligand, cyclopentadienyl(7-dimethylamino-1-diphenylphosphino-4,5,6,7-tetrahydroindenyl)iron (ptfa), and its palladium dichloride complex have been synthesised, structurally characterised by X-ray analysis of the palladium complex, and shown to be effective in the enantioselective Grignard cross coupling reaction of phenethylmagnesium chloride and vinyl bromide giving 3-phenylbut-1-ene with 79% enantiomeric excess.

Enantiomerically pure ferrocenylphosphines have proved to be excellent chiral ligands for various types of transition metal catalysts.[1] Like 2-(1-*N*,*N*-dimethylaminoethyl)-1-diphenylphosphino-ferrocene, ppfa,[2] almost all such ferrocenylaminophosphine ligands are based on 1-*N*,*N*-dimethylaminoethylferrocene as the enantiomerically pure starting material.[3] Typically, transition metal complexes of such ferrocenylaminophosphines catalyse hydrogenations, hydrosilations, and aldol-type or other carbon-carbon bond forming reactions, in many cases in high chemical and optical yields.[1] Still challenging however remains enantioselective cross-coupling as exemplified by the reaction of phenethylmagnesium chloride and vinyl bromide giving 3-phenylbut-1-ene as the product. Enantioselectivites are in general moderate for these reactions, except when either very air-sensitive chiral amino acid derivatives like t-Leuphos[4] are used or when a large excess of zinc halide is added to the reaction mixture, as in the case of ppfa[5] or similar ferrocene-based ligands.[6]

We here report the synthesis of a new enantiomerically pure ferrocenyl aminophosphine ligand, based on a homoannularly disubstituted ferrocenylamine, its palladium dichloride complex and its use for palladium-catalysed Grignard cross coupling reactions. The enantiomerically pure ferrocenylaminophosphine, cyclopentadienyl(7-dimethylamino-1-diphenylphosphino-4,5,6,7-tetrahydroindenyl)iron (ptfa) **2** was prepared by lithiation of the easily accessible (−)-ferrocene derivative[7,8] **1**, and subsequent treatment with chlorodi-



Scheme 1



Scheme 2 *Reagents and conditons:* i, BuLi–hexane (1.4 equiv.), diethyl ether, room temp., 2 h; ii, $ClPPh_2$ (2 equiv.), reflux, 3 h (77% **2**, 20% **2a**); iii, $PdCl_2(MeCN)_2$ (1 equiv.), benzene, room temp. (95%)

phenylphosphine. The air-stable homosubsituted main product **2**† was isolated in 77% yield {$[\alpha]_D^{20}$ +233 (*c* 0.456, $CHCl_3$), m.p. 186 °C}. As a byproduct, the heterosubstituted aminophosphine **2a** was isolated in 20% yield {$[\alpha]_D^{20}$ −3.3 (*c* 0.394, $CHCl_3$), orange oil}. The fact that monolithiation partly takes place at the unsubstituted cyclopentadienyl ring strongly reflects the influence of the *endo*-orientation of the dimethylamino group of **1**. Finally, **2** was treated with $PdCl_2(MeCN)_2$ in benzene to give the palladium dichloride complex **3** in 95% yield {$[\alpha]_D^{20}$ −154 (*c* 0.173, CH_2Cl_2), m.p. 205–210 °C}. The molecular structure of (±)-**3** was determined by X-ray crystallography‡ and is shown in Fig. 1. From

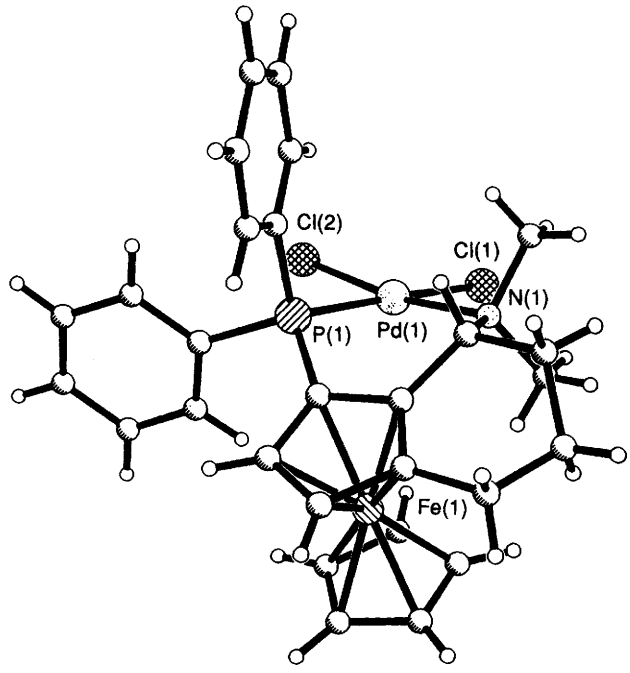


Fig. 1 Molecular structure of **3**

the known absolute configuration of **1**[7] the configuration of (−)-**3** is (*R*) at the benzylic carbon C-7 and (1*S*,7a*R*,3a*R*) for the ferrocene unit.

The air-stable and very easy to handle palladium dichloride complex **3** was found to catalyse efficiently enantioselective Grignard cross-coupling reactions. For example, in the presence of 0.4 mol% of (−)-**3**, phenethylmagnesium chloride (2 equiv.) reacts with vinyl bromide (1 equiv.) in diethyl ether (0 °C; 20 h) to give (*R*)-3-phenylbut-1-ene in 95% yield (isolated), {$[\alpha]_D^{22}$ −4.67 (neat), 79.3% enantiomeric excess (e.e)}. Thus, the enantioselectivity of **3** closely resembles that of t-Leuphos (83% e.e.), which is the highest asymmetric induction so far described for that particular Grignard cross coupling reaction. Further examples of such cross couplings are being studied, and results will be published in a full paper.

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† *NMR spectral data* of ptfa **2**: ^1H NMR ($CDCl_3$, Me_4Si, 400.1 MHz) δ 1.42 (m, 1H), 1.83 (m, 2H), 1.98 (m, 1H), 2.21 (s, 6H), 2.31 (dd, *J* −16.0, 6.5 Hz, 1H), 2.68 (ddd, *J* −16.0, 6.5, 12.4 Hz, 1H), 2.83 (m, 1H), 3.21 (m, 1H); 4.07 (s, 5H), 4.17 (m, 1H), 7.15–7.40 (m, 10H); $^{13}C\{^1H\}$ NMR ($CDCl_3$ 100.6 MHz) δ 21.0, 24.0, 24.5, 60.8 (d, $J_{C\text{-}P}$ 20.0 Hz), 67.3, 68.2 (d, $J_{C\text{-}P}$ 4.0 Hz), 71.1, 71.7 (d, $J_{C\text{-}P}$ 8.9 Hz), 86.4, 94.1, 127.3, 127.8 (d, $J_{C\text{-}P}$ 6.6 Hz), 128.1, 132.2 (d, $J_{C\text{-}P}$ 20.1 Hz), 134.5 (d, $J_{C\text{-}P}$ 21.3 Hz), 140.2 (d, $J_{C\text{-}P}$ 16.2 Hz), 140.2 (d, $J_{C\text{-}P}$ 12.6 Hz); $^{31}P\{^1H\}$ NMR ($CDCl_3$, 85% H_3PO_4, 162.0 MHz) δ −16.4.

‡ *Crystal structure analysis of* (±)-**3**: data collected at 90 K; space group $P2_1/n$, $Z = 4$ for $C_{28}H_{30}Cl_2FeNPPd$, $M_r = 644.65$. $a = 15.996(16)$, $b = 9.987(9)$, $c = 16.129(14)$ Å, $\beta = 95.82(7)°$, $V = 2563.4(1.2)$ Å^3, $D_c = 1\ 67$ g cm^{-3}. Intensity data were collected for two octants with $5.5 \leqslant 2\theta\ 55°$, 6588 observed, 5749 unique, and 4005 significant [$F_{obs} > 4\sigma(F)$] structure factors. Structure refined with anisotropic atomic displacement parameters for all non-hydrogen atoms, H atoms at calculated positions, $R = 0.0432$ (unit weights) for 307 parameters and 4005 observations. A final difference Fourier synthesis showed features up to 0.9(1) e Å^{-3} in the vicinity of the metal atoms. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

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