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Palladium complexes of bulky *ortho*-trifluoromethylphenyl-substituted phosphines: Unusually regioselective catalysts for the hydroxycarbonylation and alkoxycarbonylation of alkenes

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ABSTRACT

The reactions of the very bulky phosphine ligands containing both *tert*-butyl and *ortho*-trifluoromethylphenyl substituents with $[PdCl_2(PhCN)_2]$ have been studied, in order to assess the impact of steric and electronic effects on a ligand's coordination ability. The palladium complexes of *tert*-butyl(*ortho*-trifluoromethylphenyl)methyl phosphine and *tert*-butyl(*ortho*-trifluoromethylphenyl)(*n*-butyl)phosphine were characterised by X-ray crystallography and shown to be good precatalysts for the hydroxy- and alkoxycarbonylation of alkenes relative to Pd complexes of tricyclohexylphosphine and triphenylphosphine. A notable feature of Pd complexes of *tert*-butyl(*ortho*-trifluoromethylphenyl)methyl phosphine is significantly enhanced regioselectivity relative to previous state-of-the-art catalysts in the hydroxycarbonylation of styrene, even if lithium chloride co-catalysts are not used. These catalysts derived from large cone angle ligands consistently give higher regioselectivity in the alkoxycarbonylation of styrene using ethanol, *n*-propanol, and i-propanol as nucleophiles. These Pd complexes are also active in the Suzuki coupling of activated aryl chlorides, and in both carbonylation and Suzuki reactions, *tert*-butyl(*ortho*-trifluoromethylphenyl)methyl phosphine gives more productive catalysts than its bulkier analogues.

1. Introduction

Bulky phosphorus ligands have become increasingly important in homogeneous catalysis and organometallic chemistry as they often radically alter the properties of late transition metal complexes. This is particularly striking in carbonylation catalysis where bulky monophosphines give enhanced activity in hydroformylation, and where bulky diphosphines give enhanced regio- and/or enantio-selectivity [1]. Bulky diphosphines have also given remarkable results in alkoxycarbonylations of terminal alkenes [2]. We have recently reported the use of Pd complexes of the new bidentate ligands, **1**–**4** as highly regioselective and active catalysts for hydroxycarbonylation of styrene [3]. However, alkyl monophosphines have generally been considered as relatively poor ligands for Pd catalysed hydroxycarbonylation based on the inactivity of Me_3P and Cy_3P and the lower activity (but greater regioselectivity) observed with ligands such as Ph_2P(*o*-tolyl) [4] (Fig. 1).

There is very sparse data available on phosphines that contain both bulky *ortho*-trifluoromethylphenyl groups and *tert*-butyl groups [5], and in the preliminary report on the bidentate ligands, **1**–**5**, we noted that ligand **5** failed to coordinate to any transition metals at all. Evidently, ligands with this combination of *tert*-butyl and *ortho*-trifluoromethylphenyl groups are finely balanced between coordinating as bulky ligands and being inert to transition metals. In order to clarify the importance of steric and electronic factors within these unusual bulky phosphines, we elected to study some simple but previously unstudied monophosphines that contain both very bulky *ortho*-trifluoromethylphenyl groups and electron donating alkyl groups. In this paper, we report the synthesis of these ligands, their palladium(II) complexes and the somewhat surprising finding that Pd complexes of (*tert*-butyl)methyl(*ortho*-trifluoromethylphenyl)phosphine give improved regioselectivity relative to other ligands when used as catalyst for hydroxy- and alkoxycarbonylations of a range of vinyl arenes.

2. Experimental

2.1. General experimental procedures and instrumentation

Routine NMR data were recorded either on a Bruker Avance 300 (^{1}H at 300 MHz, ^{13}C at 75 MHz, ^{19}F at 282 MHz, ^{31}P at 121 MHz) or a Bruker Avance II 400 (^{1}H at 400 MHz, ^{13}C at 100 MHz, ^{19}F at 376 MHz, ^{31}P at 161 MHz). ^{1}H and ^{13}C spectra were referenced to

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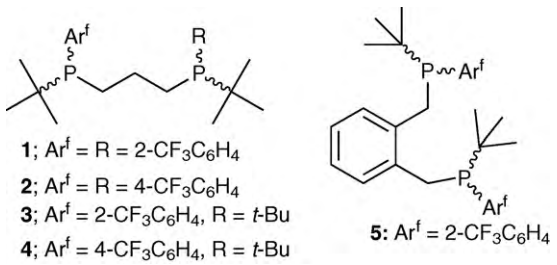


Fig. 1. Bulky bidentate ligands either give highly regioselective Pd catalysts or are too bulky to act as ligands.

external tetramethylsilane, ^{19}F spectra were referenced to external trichlorofluoromethane, and ^{31}P spectra were referenced to external phosphoric acid. Chemical shifts are expressed in parts per million. Chemical ionisation mass spectroscopy and electron ionisation mass spectroscopy were performed on a Micromass GCT spectrometer. Electrospray mass spectroscopy was performed on a Micromass LCT spectrometer. All were operated by Mrs Caroline Horsburgh. Infra-red spectra were recorded on a Perkin Elmer GX-FTIR System spectrometer. Thin layer chromatography was performed using 0.20 mm layers of silica gel supported on plastic sheets (Macherey-Nagel, Polygram Sil G/UV_{254}) or using 0.20 mm layers of aluminium oxide supported on plastic sheets (Merck Aluminium oxide F_{254}). Preparative chromatography was performed using Davasil silica gel 35–70 μm. Dry degassed diethyl ether, petroleum ether, THF and toluene were obtained from an Innovative Technologies Puresolve 400 solvent still. Other solvents were bought and used as received without further purification other than degassing by either purging with nitrogen or repeated freeze/thaw cycles under vacuum. Organic solutions were dried by standing over anhydrous sodium sulphate and evaporated either under reduced pressure on a rotary evaporator or under reduced pressure whilst agitating manually. *tert*-Butyldichlorophosphine was obtained from the Aldrich Chemical Company and used as received. All manipulations were carried out under an atmosphere of nitrogen unless otherwise stated.

2.2. (*o*-Trifluoromethylphenyl)(tert-butyl)methylphosphine **7**

(*ortho*-Trifluoromethyphenyl)*tert*-butylchlorophosphine (0.318 g, 1.18 mmol) was dissolved in diethyl ether (10 mL) and cooled to −78 °C. MeLi (1.38 mL, 2.208 mmol, 1.6 equivalents as a 1.6 M solution in hexanes) was added slowly and the reaction allowed to warm to room temperature gradually over 3 h. The solvent was then removed under vacuum to near dryness and degassed CH_2Cl_2 (15 mL) added. The reaction was then quenched with degassed water (2 mL) which was then removed by syringe, and the remaining CH_2Cl_2 layer dried using Na_2SO_4 which was filtered off. The solvent was then removed to give the product as an air sensitive light brown oil (165 mg, 0.665 mmol) in 56% yield.

^1H NMR (300 MHz; C_6D_6): δ 7.6–7.8 (2 H, d, *J* = 15.2 Hz, ArH), 7.55 (1 H, t, app., *J* = 7.0 Hz, ArH), 7.47 (1 H, t, app., *J* = 7.8 Hz, ArH), 1.18 (3 H, d, *J* = 15.2 Hz, P-CH_3), 1.04 (9 H, d, *J* = 12.3 Hz, $C(CH_3)_3$. $^{13}C\{^1H\}$ NMR (75 MHz; C_6D_6): δ 138.2 (d, *J* = 39 Hz, ArC-P), 136.6 (q d, *J* = 31 Hz, *J* = 2 Hz, ArC-CF_3), 134.5 (d, *J* = 4 Hz, ArCH *o*-P), 130.9 (s, ArCH), 130.9 (s, ArCH), 129.5 (s, ArCH), 126.7 (dq, *J* = 6 Hz, *J* = 6 Hz, ArCH *o*-CF_3), 125.4 (q, *J* = 278 Hz, CF_3), 29.8 (d, *J* = 15 Hz, $C(CH_3)$), 29.6 (d, *J* = 17 Hz, CH_3 methyl), 27.7 (d, *J* = 15 Hz, CH_3 *tert*-butyl). ^{19}F NMR (282 MHz; C_6D_6): δ −54.9 (d, *J* = 58 Hz), ^{31}P NMR (121 MHz; C_6D_6): δ −20.0 (q, *J* = 58 Hz). MS CI+: *m*/*z* 249.0 ($[M+H]^+$ requires 249.09).

2.3. *n*-Butyl(*t*-butyl)(*o*-trifluoromethylphenyl)phosphine, **8**

The same procedure used in the preparation of **7** was followed. From *n*-Butyl(*t*-butyl)(*o*-trifluoromethylphenyl)phosphine-borane (300 mg, 0.98 mmol) the title compound was obtained as a yellowish oil. Yield: 203 mg (71%).^1H NMR (300 MHz, $CDCl_3$): δ 7.77–7.70 (m, 2H, ArH), 7.85–7.82 (m, 1H, ArH), 7.55–7.43 (m, 2H, ArH), 1.98–1.87 (m, 1H, C*H*H), 1.74–1.61 (m, 1H, CH*H*), 1.38–1.28 (m, 3H, CH_2, C*H*H), 1.12 (m, 1H, CH*H*), 1.02 (d, 9H, *J* = 12.1 Hz), 0.83 (t, 3H, *J* = 6.9 Hz). $^{13}C\{^1H\}$NMR (75 MHz, $CDCl_3$): δ 133.9 (d, CH, *J* = 3.5 Hz), 130.4 (CH), 129.0 (CH), 126.3 (m, CH), 28.5 (d, CH_2, *J* = 16.6 Hz), 27.9 (d, CH_3, *J* = 14.3 Hz), 24.4 (d, CH_2, *J* = 12.5 Hz), 22.3 (d, CH_2, *J* = 17.9 Hz), 13.8 (s, CH_3). $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$): δ −8.1 (q, *J* = 56.0 Hz). $^{19}F\{^1H\}$NMR (282 MHz, $CDCl_3$): δ −55.2 (d, *J* = 74.8 Hz). MS (ES+): 313 ($M+Na^+$); HRMS calcd. for $C_{15}H_{23}F_3P$, 291.1489; found 291.1495.

2.4. (*O*-trifluoromethylphenyl)(t-butyl)methylphosphineborane, **9**

It is generally possible to generate the phosphine directly in >95% purity, but if further purification is required, a more stable borane complex can be prepared as shown below.

2.5. From t-butyl(*o*-trifluoromethylphenyl)chlorophosphine (Route A)

t-Butyl(*o*-trifluoromethylphenyl)chlorophosphine (669 mg, 2.49 mmol) was dissolved in 20 mL of diethyl ether and the solution cooled to −78 °C. MeLi (3.25 mL of a 1.6 M solution in diethyl ether, 5.2 mmol) was added and the mixture was allowed to warm to room temperature overnight. The mixture was then cooled to 0 °C and BH_3·THF (6.2 mL of a 1 M solution in THF, 6.2 mmol) was quickly added. The mixture was warmed to room temperature and stirred for 2 h. A few drops of water were carefully added to quench the excess of MeLi and subsequently the mixture was subjected to extractive work-up (water/diethyl ether). The crude material after concentration to dryness was purified by column chromatography (SiO_2, hexane/Et_2O, 80/20). The desired product was isolated as a white microcrystalline powder with purity of around 98% after vacuum removal of the solvents. Yield: 370 mg (57%).

2.6. From t-butyl(*o*-trifluoromethylphenyl)phosphine-borane (Route B)

t-Butyl(*o*-trifluoromethylphenyl)phosphine-borane (496.2 mg, 2.0 mmol) were dissolved in 15 mL of THF and the solution cooled to −78 °C. *n*-BuLi (880 μL of a 2.5 M solution in hexanes, 2.2 mmol) were dissolved in 10 mL of diethyl ether and this solution added over 1 h to the phosphine-borane solution. After the addition, the solution was slowly warmed to 0 °C and cooled back to −78 °C. Methyl iodide (162 μL, 2.6 mmol) were added and the solution was allowed to warm to room temperature overnight. The solvents were then removed under vacuum and the crude product was purified by column chromatography in similar fashion to Route A and generally gave material with purity >99%. Yield: 357 mg (68%).

^1H NMR (400 MHz, $CDCl_3$): δ 8.30 (dd, 1H, *J* = 14.0 Hz, 7.3 Hz), 7.85–7.83 (m, 1H), 7.66–7.58 (m, 2H), 1.80 (dd, 3H, H, *J* = 10.1 Hz, 2.0 Hz), 1.14 (d, 9H, H, *J* = 14.3 Hz), 1.80–0.10 (br, q, 3H, BH_3). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 139.5 (d, CH, *J* = 16.7 Hz), 132.0–122.0 (m, CH), 127.3 (q, CF_3, *J* = 6.9 Hz), 30.6 (d, *J* = 30.7 Hz), 26.0 (d, CH_3, *J* = 15.0 Hz), 29.6 (dd, CH_3, *J* = 35.7 Hz, 6.7 Hz). $^{31}P\{^1H\}$NMR (162 MHz, $CDCl_3$): δ +35.5 (q, *J* = 56.6 Hz). $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$): δ −55.9 (s). ^{11}B NMR (128 MHz, $CDCl_3$): δ −36.6 (m). MS (ES+): 285 ($M+Na^+$); HRMS calcd. for $C_{12}H_{19}BF_3NaP$, 285.1167; found 285.1166.

These boranes can be converted into the free phosphine by reaction with HBF_4. (*ortho*-Trifluoromethylphenyl)(*tert*-butyl)methylphosphineborane (262 mg, 1.0 mmol) was dissolved in 10 mL of dichloromethane and the solution cooled to −30 °C. $HBF_4{\cdot}OMe_2$ (0.350 mL, 2.9 mmol) was added and the mixture was allowed to warm to room temperature overnight. ^{31}P NMR spectroscopy indicated the total conversion to the phosphonium salt (d = +20 ppm). The reaction mixture was treated with 30 mL of previously degassed saturated aqueous solution of $NaHCO_3$ and the organic layer was extracted with dichloromethane under argon. The combined organic extracts were dried with sodium sulfate and filtered. Concentration to dryness under vacuum afforded the desired product as a yellow/brown oil. Yield: 170 mg (68%).

2.7. n-Butyl(t-butyl)(o-trifluoromethylphenyl)phosphine-borane, **10**

The same procedure used in the preparation of **9** (Route A) was followed, employing *n*-BuLi solution in hexanes instead of MeLi. From *t*-butyl(*o*-trifluoromethylphenyl)chlorophosphine (927 mg, 3.45 mmol) and *n*-BuLi (2.9 mL of a 2.5 M solution, 7.25 mmol) the title compound was obtained after chromatography as a colourless oil with purity ranging from 95 to 99%. Yield: 313 mg (30%).

^1H NMR (400 MHz, $CDCl_3$): δ 8.27–8.21 (m, 1H), 7.85–7.82 (m, 2H), 7.64–7.52 (m, 2H), 2.36 (m, 1H), 1.92–1.83 (m, 1H), 1.81–1.69 (m, 1H), 1.45–1.37 (m, 2H), 1.31–1.25 (m, 1H), 1.13 (d, 9H, J = 13.8 Hz), 0.90 (t, 3H, J = 7.4 Hz), 1.80–0.10 (br, q, 3H, BH_3). $^{13}C\{^1H\}$NMR- (101 MHz, $CDCl_3$): δ 139.9 (d, CH, J = 18.0 Hz), 131.2 (CH), 131.1 (CH), 128.0 (t, CH, J = 7.9 Hz), 125.3 (m, CF_3), 31.2 (d, C, J = 38.9 Hz), 26.6 (s, CH_2), 25.4 (d, CH_2), 24.5 (d, CH_2, J = 19.5 Hz), 20.9 (dd, CH_3, J = 42.4 Hz, 5.9 Hz), 13.6 (s, CH_3). $^{31}P\{^1H\}$NMR (162 MHz, $CDCl_3$): δ +43.2 (d, J = 71.9 Hz). $^{19}F\{^1H\}$NMR (376 MHz, $CDCl_3$): δ −56.0 (s). ^{11}B NMR (128 MHz, $CDCl_3$): δ −37.4 (m).

MS (ES+): 327 ($M+Na^+$); HRMS calcd. for $C_{15}H_{25}BF_3NaP$, 327.1637; found 327.1630.

2.8. tert-Butylbis(o-(trifluoromethyl)phenyl)phosphine **11**

A stirred solution of *ortho*-bromobenzotrifluoride (8.49 g, 5.26 mL, 37.7 mmol) diethyl ether (40 mL) was cooled to −78 °C, and *n*-butyllithium (15 mL as a 2.5 M solution in hexanes, 37.7 mmol) added slowly, after which the reaction was allowed to warm to room temperature. The solution was then cooled to −78 °C and *t*-butyldichlorophosphine (2.00 g as a solution in 10 mL diethyl ether, 12.57 mmol) added slowly by dropping funnel. The solution was then allowed to warm slowly to room temperature. After 16 h the dark green solution was washed with water. The diethyl ether layer retained and dried with $MgSO_4$, filtered and the solvent removed. Recrystalisation from methanol yielded the product as air stable white crystals (3.880 g, 10.25 mmol) in 82% yield.

^1H NMR (300 MHz; C_6D_6): δ 7.75 (2 H, d m, J = 7.5 Hz, ArH *o*-CF_3), 7.6 (2H, ddd, J = 5.3 Hz, J = 8 Hz, ArH *o*-P), 7.4 (2H, td, J = 7.5 Hz, ArH), 7.32 (2H, td, J = 7.5 Hz, ArH), 1.2 (9H, d, J = 13.3, $(CH_3)_3$). $^1H\{^{31}P\}$ NMR (300 MHz; C_6D_6): δ 7.75 (2 H, dm, J = 7.5 Hz, ArH *o*-CF_3), 7.6 (2H, dd, J = 8 Hz, ArH *o*-P), 7.4 (2H, td, J = 7.5 Hz, ArH), 7.32 (2H, td, J = 7.5 Hz, ArH), 1.2 (9 H, s, $(CH_3)_3$). $^{13}C\{^1H\}$ NMR (100 MHz; $CDCl_3$): δ 136.1 (d, J = 40 Hz, ArCH), 136.0 (s, ArCH), 135.3 (m, ArC-CF_3), 130.5 (s, ArCH), 128.5 (s, ArCH), 127.2 (m, ArCH *o*-CF_3), 124.2 (q, J = 275 Hz, CF_3), 31.7 (d, J = 21 Hz, P-$C(CH_3)_3$), 29.3 (d, J = 16 Hz, CH_3). ^{19}F NMR: δ −55.8 (d, J = 51.1 Hz), $^{31}P\{^1H\}$ NMR: δ −2.6 (sep, J = 51.2 Hz), IR (cm^{-1}), KBr, 3050, 2900–3000, 2200, 1300. MS ES+: m/z 401.02 ($[M+Na]^+$ requires 401.09). Anal. Calcd. for $C_{18}H_{17}F_6P$: C, 57.15; H, 4.53% found: C, 56.66; H, 4.73%.

2.9. Bis((o-trifluoromethylphenyl)tert-butylmethylphosphine)palladiumdichloride, **12**

(*ortho*-Trifluoromethylphenyl)*tert*-butylmethylphosphine (55 mg, 0.220 mmol) was dissolved in dry degassed CH_2Cl_2 (2 mL). $[PdCl_2(PhCN)_2]$ (42 mg, 0.110 mmol) was added and the mixture stirred at room temperature for 24 h. The solvent was then reduced to near dryness and diethyl ether added resulting in a yellow precipitate, which was filtered off and washed with further diethyl ether to yield the title compound (45 mg, 73 mmol, 67% yield). The complex is present as a mixture of the *rac* and *meso* isomers leading to two sets of signals in the ratio 1:2.5 by ^{19}F NMR. Recrystallisation by slow diffusion of hexane into a CH_2Cl_2solution of the product yielded crystals suitable for X-ray crystallography.

^1H NMR (400 MHz; CD_2Cl_2): δ 7.79 (2H, m, ArH), 7.69 (2 H, m, ArH), 7.49 (4H, m, ArH), 1.86 (3H, t app., J = 7.4 Hz, P-CH_3 major isomer), 1.85 (3H, t app., J = 7.4 Hz, P-CH_3 minor isomer), 1.21 (9 H, t app., J = 7.4 Hz, $C(CH_3)_3$ minor isomer), 1.20 (9 H, t app., J = 7.4 Hz, $C(CH_3)_3$ major isomer). $^1H\{^{19}F\}$NMR (400 MHz; CD_2Cl_2): δ 7.79 (1H, m, ArH), 7.69 (1 H, m, ArH), 7.49 (2H, m, ArH), 1.86 (3H, t app., J = 7.4 Hz, P-CH_3 major isomer), 1.85 (3H, t app., J = 7.4 Hz, P-CH_3 minor isomer), 1.21 (t app., J = 7.4 Hz, $C(CH_3)_3$ minor isomer), 1.20 (t app., J = 7.4 Hz, $C(CH_3)_3$ major isomer). $^1H\{^{31}P\}$ NMR (400 MHz; CD_2Cl_2): δ 7.79 (1H, m, ArH), 7.69 (1 H, m, ArH), 7.49 (2H, m, ArH), 1.86 (3H, s, P-CH_3 major isomer), 1.85 (3H, s, P-CH_3 minor isomer), 1.21 (s, $C(CH_3)_3$ minor isomer), 1.20 (s, $C(CH_3)_3$ major isomer).$^{13}C\{^1H\}$ NMR (101 MHz; CD_2Cl_2): δ 134.7 (m, ArCH), 132.0 (m, ArC), 129.4 (m, ArCH), 129.2 (s, ArCH), 128.9 (m, ArC), 127.5 (m, ArCH), 123.5 (q, J = 275.5 Hz, CF_3), 34.6 (t app., J = 11.1 Hz, $C(CH)_3$ major isomer), 34.4 (t app., J = 11.1 Hz, $C(CH)_3$, minor isomer), 26.8 (m, $C(CH)_3$), 8.2 (m, P-CH_3). ^{19}F NMR (376 MHz; CD_2Cl_2): δ −52.95 (t, J = 6.9 Hz, major isomer), −53.1 (t, J = 6.9 Hz, minor isomer). ^{31}P NMR (162 MHz; CD_2Cl_2): δ 27.4 (m). IR (cm^{-1}), KBr, 3200, 3500, 2900–3000, 2200, 1300. MS ES+ 697.02 (M+Na). Calcd. for $C_{24}H_{23}Cl_2F_6P_2Pd$, C 42.78%, H 4.79%; found: C 42.65%, H 4.74%.

2.10. Bis[n-butyl(t-butyl)(o-trifluoromethylphenyl)phosphine]palladiumdichloride, **13**

The same procedure used in the preparation of **5** was followed. From **4** (180 mg, 0.62 mmol) the title compound was obtained an orange solid. Yield: 63 mg (28%). X-ray diffraction: crystals suitable for X-ray diffraction were grown by slow diffusion of hexane into a dichloromethane solution of the product at room temperature.

^1H NMR (500 MHz, CD_2Cl_2): δ 8.16 (m, 2H, minor); 8.08 (m, 2H, major), 7.76–7.72 (m, 2H), 7.62–7.53 (m, 4H), 2.57–2.48 (m, 4H), 2.16–2.09 (m, 2H), 1.92–1.85 (m, 2H), 1.56–1.49 (m, 4H), 1.25–1.22 (m, 18H), 1.02 (t, 6H, J = 7.4 Hz, major), 0.98 (t, 6H, J = 7.4 Hz, major). $^{13}C\{^1H\}$ NMR (125 MHz, CD_2Cl_2): δ 138.2 (CH, minor), 137.7 (CH, major), 133.2–132.8 (m, C), 131.0–132.8 (m, C), 130.4 (d, CH, J = 3.7 Hz, minor), 130.4 (d, CH, J_{CP} = 3.7 Hz, major), 123.4 (CH, major), 123.4 (CH, minor), 36.9–36.6 (m, C); 31.0 (s, CH_2), 30.8 (s, CH_2), 28.6 (s, CH_3), 28.1 (s, CH_3, 25.4–25.2 (m, CH_2), 23.4 (m, CH_2), 14.0 (s, CH_3). $^{31}P\{^1H\}$ NMR (202 MHz, CD_2Cl_2): δ +39.4 (s, br). $^{19}F\{^1H\}$ NMR (470 MHz, CD_2Cl_2): δ −53.6 (major, br); −53.7 (minor, br). MS (EI): 776 ($M+NH_4^+$), 722 (M−Cl). Calcd. for $C_{30}H_{44}Cl_2F_6P_2Pd$, C 47.54%, H 5.85%; found: C 47.52%, H 5.76%.

2.11. Procedure for hydroxycarbonylation

A Biotage 2 mL microwave vial containing a stirring bar was charged with the appropriate amounts of LiCl, *para*-toluenesulfonic acid, catalyst and substrate if the latter was a solid. The vial

Table 1
Hydroxycarbonylation of vinyl arenes.

Entry[a]	Substrate	Catalyst [% Pd][a]	LiCl (%)	PTSA (%)	Time (h)	Conv.[b] %	*b*:l[c]	Yield[d] %
1	Styrene, 16	14, 1.0	20	20	6	95	86:1	59
2	Styrene	15, 1.0	20	20	6	32	>200:1	8
3	Styrene	12, 1.0	20	20	6	>99	>200:1	55
4	Styrene	13, 1.0	20	20	6	69	>200:1	32
5	Styrene	14, 0.5	5	5	6	81	76:1	40
6	Styrene	15, 0.5	5	5	6	51	>200:1	2
7	Styrene	12, 0.5	5	5	6	77	>200:1	51
8	Styrene	13, 0.5	5	5	6	10	–	0
9	Styrene	14, 1.0	0	10	24	>99	8.7:1	71
10	Styrene	12, 1.0	0	10	24	54	>200:1	37
11	Styrene	14, 0.5	0	5	16	>99	9.9:1	63
12	Styrene	15, 0.5	0	5	16	55	120:1	35
13	Styrene	12, 0.5	0	5	16	32	>200:1	19
14	Styrene	13, 0.5	0	5	16	3	>200:1	1
15	17	14, 0.5	5	5	24	>99	100:1	85
16	17	12, 0.5	5	5	24	>99	>200:1	77
17	17	13, 0.5	5	5	24	16	>200:1	10
18	18	14, 0.5	5	5	24	>99	67:1	57
19	18	12, 0.5	5	5	24	85	>200:1	41
20	19	14, 0.5	5	5	24	90	46:1	59
21	19	12, 0.5	5	5	24	>99	>200:1	88

[a] Reactions carried out at 30 bar of CO, at 80 °C, in 1.5 mL of degassed butanone in presence of 2.5 equivalents (with respect to styrene) of degassed water, using the $[PdCl_2(L)_2]$ precatalysts.
[b] ^{1}H NMR spectroscopy of reaction mixtures before work-up does not reveal any side products, hence, conversion is calculated as acids/(acids + styrene) × 100 determined.
[c] Ratio of branched/linear acid in the isolated products determined by ^{1}H NMR integration.
[d] Isolated yield of pure acids.

was sealed with a crimp cap, purged with three vacuum/argon cycles and left under argon atmosphere. The substrate (if a liquid), degassed water and degassed butanone (1.5 mL) were added with syringe. Two needles were pierced into the vial and this was introduced into the autoclave, which had been previously purged with three vacuum/argon cycles. The autoclave was then purged three times with CO, pressurised to 30 bar and immersed into an oil bath preheated to the desired temperature. After the desired reaction time, the autoclave was cooled down to room temperature, the pressure slowly released and opened. A small sample was taken and analysed by ^{1}H NMR to calculate the conversion. The contents of the vial were then diluted with toluene and extracted three times with saturated aqueous $NaHCO_3$ solution. The combined aqueous layers were acidified with concentrated HCl until decidedly acidic pH according to litmus paper. This solution was then extracted with dichloromethane and the combined organic phases dried with $MgSO_4$, filtered and the final solution concentrated to dryness under vacuum. The residue consisted in the pure acid.

2-Phenylpropanoic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.15 (m, 5H), 3.65 (q, 1H, J = 7.2 Hz), 1.43 (d, 3H, J = 7.2 Hz). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 180.8 (C=O), 139.8 (C), 128.7 (CH), 127.7 (CH), 127.4 (CH), 45.4 (CH), 18.1 (CH_3).

MS (ES+): 173 ($M+Na^+$); (ES−): 149 (M−H).

2-(4-tert-Butylphenyl)propanoic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, 2H, J = 8.3 Hz), 7.26 (d, 2H, J = 8.3 Hz), 3.72 (q, 1H, J = 7.2 Hz), 1.51 (d, 3H, CH_3 J = 7.2 Hz); 1.31 (s, 9H, Bu^t). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 181.0 (C=O), 150.3 (C), 136.7 (C), 127.3 (2xCH), 125.6 (2xCH), 44.9 (CH), 34.5 (C), 31.3 (3xCH_3), 18.0 (CH_3).

MS (ES−): 205 (M−H).

2-(6-Methoxy-2-naphthyl)propanoic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, 1H, J = 2.0 Hz), 7.69 (m, 2H), 7.41 (dd, 1H, J = 8.5 Hz, 1.9 Hz), 7.14 (dd, 1H, J = 8.9 Hz, 2.6 Hz), 7.11–7.10 (m, 1H); 3.91 (s, 3H), 3.88 (q, 1H, J = 7.2 Hz), 1.59 (d, 3H, J = 7.2 Hz)

$^{13}C\{^1H\}$ NMR: (101 MHz, $CDCl_3$): δ 180.5 (C=O), 157.7 (C), 134.9 (C), 133.8 (C), 129.3 (CH), 128.9 (C), 127.3 (CH), 126.2 (CH), 126.2 (CH), 119.1 (CH), 105.6 (CH), 55.3 (CH_3), 45.2 (CH), 18.1 (CH_3). MS (ES+): 253 ($M+Na^+$); (ES−): 229 (M−H); HRMS calculated for $C_{14}H_{14}NaO_3$, 253.0841; found 253.0847.

Indan-1-carboxylic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, 1H, J = 7.0 Hz), 7.15–7.10 (m, 3H), 3.98 (dd, 1H, J = 8.4 Hz, 6.1 Hz), 3.06–2.98 (m, 2H), 2.87–2.79 (m, 2H), 2.40–2.31 (m, 2H), 2.30–2.21 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 180.7 (C=O), 144.2 (C), 140.1 (C), 127.8 (CH), 126.6 (CH), 125.0 (CH), 124.8 (CH), 50.1 (CH), 31.8 (CH_2), 28.7 (CH_2). MS (ES−): 161 (M−H), HRMS calculated for $C_{10}H_9O_2$ 161.0603; found 161.0608.

2.12. Procedure for alkoxycarbonylation

A Biotage 2 mL microwave vial containing a stirring bar was charged with the appropriate amounts of LiCl, *para*-toluenesulfonic acid and catalyst. The vial was sealed with a crimp cap, purged with three vacuum/argon cycles and left under argon atmosphere. Styrene, tetraethylsilane (internal standard) and the appropriate degassed alcohol (1.5 mL) were added with syringe. Two needles were pierced into the vial and this was introduced into the autoclave, which had been previously purged with three vacuum/argon cycles. The autoclave was then purged three times with CO, pressurised to 30 bar and immersed into an oil bath preheated to 80 °C. After 24 h, the autoclave was cooled down to room temperature, the pressure slowly released and opened. A small sample was taken and analysed by ^{1}H NMR to calculate the conversion. The contents of the vials were vacuumed down to dryness, yielding a yellowish gummy material, which was suspended in EtOAc/hexane (1:1) and filtered through a small plug of SiO_2. The solvents (and any styrene) were then removed under vacuum yielding the pure desired ester. Regioselectivities of >200:1 refer, except in the case of Table 1, entries 17 (270:1) and 21 (370:1), refer to regioisomerically pure products.

Ethyl 2-phenylpropanoate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.15 (m, 5H), 4.11–3.98 (m, 2H), 3.63 (q, 1H, J = 7.2 Hz), 1.42 (d, 3H, J = 7.2 Hz), 1.13 (t, 3H, J = 7.1 Hz). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 174.6 (C=O), 140.7 (C); 128.6 (CH), 127.5 (CH), 127.1 (CH), 60.7 (CH_2), 45.6 (CH), 18.6 (CH_3), 14.1 (CH_3).

MS (ES+): 201 ($M+Na^+$); HRMS calculated for $C_{11}H_{14}NaO_2$, 201.0891; found 201.0887

Propyl 2-phenylpropanoate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25–7.11 (m, 5H), 3.94 (t, 2H, J = 6.7 Hz), 3.64 (q, 1H, J = 7.2 Hz),

1.55–1.47 (m, 2H), 1.42 (d, 3H, J = 7.2 Hz), 0.77 (t, 3H, J = 7.4 Hz). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 174.6 (C=O), 140.7 (C), 128.6 (CH), 127.5 (CH), 127.1 (CH), 66.3 (CH_2), 45.6 (CH), 21.9 (CH_2), 18.5 (CH_3), 10.2 (CH_3). MS (ES+): 215 ($M+Na^+$); HRMS calculated for $C_{12}H_{16}NaO_2$, 215.1048; found 215.1042.

Isopropyl 2-phenylpropanoate: ^1H NMR (300 MHz, $CDCl_3$): δ 7.35–7.21 (m, 5H), 5.05–4.93 (m, 1H), 3.67 (q, 1H, J = 7.2 Hz), 1.48 (q, 3H, J = 7.2 Hz), 1.22 (d, 3H, J = 6.3 Hz), 1.13 (d, 3H, J = 6.3 Hz). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 174.9 (C=O), 141.5 (C), 128.9 (CH), 127.9 (CH), 127.4 (CH), 68.4 (CH), 46.2 (CH), 22.2 (CH_3), 22.0 (CH_3), 19.0 (CH_3). MS (ES+): 215 ($M+Na^+$).

2.13. Procedure for Suzuki–Miyaura coupling: preparation of 4-(4-fluorophenyl) acetophenone

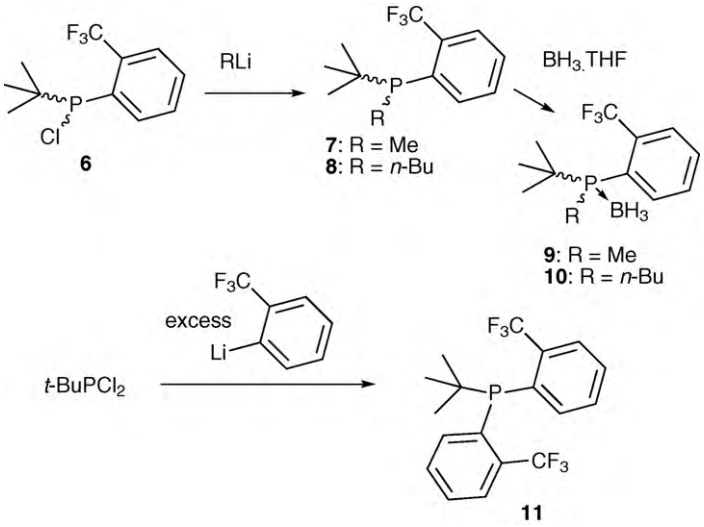
A clean dry *Schlenk* tube was charged with the catalyst (0.5 mol%), 4-fluorophenylboronic acid (105 mg, 0.75 mmol) and potassium triphosphate (318 mg, 1.5 mmol). The *Schlenk* tube was purged and the air displaced with argon before the addition of dry and degassed toluene (3 mL) followed by 4-chloroacetophenone (65 μL, 0.5 mmol). The *Schlenk* tube was immersed into a preheated oil bath at 90 °C. After the desired reaction time, the reaction mixture was cooled down to room temperature and a small sample taken and analysed by ^1H NMR. If full conversion was achieved, the reaction mixture was filtered through a plug of silica and the solution concentrated under vacuum to afford the desired biaryl as a white solid. Alternatively, the reaction mixture was concentrated *in vacuo* and purified by flash column chromatography.

4-(4-Fluorophenyl)acetophenone: ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, 2H, J = 8.6 Hz), 7.64 (d, 2H, J = 8.6 Hz), 7.61–7.58 (m, 2H), 7.19–7.13 (m, 2H), 2.64 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 198.1 (C=O), 163.0 (d, C, J = 248.2 Hz), 144.7 (C), 136 (d, CH, J = 3.3 Hz), 135.9 (C), 129.0 (CH), 128.9 (CH), 127.1 (CH), 115.9 (d, CH, J = 21.6 Hz), 26.7 (CH_3). $^{19}F\{^1H\}$ NMR (282 MHz, $CDCl_3$): δ −114.47. MS (EI): 214 (M^+); 199; 170; 85

Crystallographic data: X-ray diffraction studies for **12** and **13** were performed at 93 K using a Rigaku MM007/Mercury diffractometer (confocal optics Mo-Kα radiation). Intensity data were collected using ω steps accumulating area detector frames spanning at least a hemisphere of reciprocal space for all structures (data were integrated using CrystalClear). All data were corrected for Lorentz, polarisation and long-term intensity fluctuations. Absorption effects were corrected on the basis of multiple equivalent reflections. Structures were solved by direct methods and refined by full-matrix least-squares against F^2 (SHELXTL) Hydrogen atoms were assigned riding isotropic displacement parameters and constrained to idealised geometries. Tables of bond lengths and angles, along with crystallographic experimental can be found in the supporting information (PDF file). CCDC761532 and CCDC761533 contain the supplementary crystallographic data for compounds, **12** and **13**, respectively as CIF files. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

3. Results and discussion

The preparation of the new ligands, **7**, **8**, and **11** is straightforward. (*tert*-butyl)methyl(*ortho*-trifluoromethylphenyl)phosphine, **7** was prepared from the chlorophosphine **6** by the addition of an excess of methyllithium (Scheme 1). The reaction proceeded cleanly to give a very air sensitive oil with the ^{31}P NMR spectrum showing no significant impurities. The ^{19}F NMR spectrum displays a doublet at 55.2 ppm due to the ^4J coupling to phosphorus (J_{F-P} 57 Hz). The corresponding coupling is seen in the quartet observed in the $^{31}P\{^1H\}$ NMR spectrum at



Scheme 1. Synthesis of the new bulky monophosphines, **9**–**11**.

−20.0 ppm. This phosphine can be prepared direct from Bu^tPCl_2 by successive treatments with *ortho*-trifluoromethylphenyl lithium and methyl lithium (without isolation of the chlorophosphine intermediate), and can also be prepared from (*tert*-butyl)(*ortho*-trifluoromethyl-phenyl)phosphine-borane by lithiation and reaction with methyl iodide, followed by deprotection of the borane, **9** in a subsequent step. (*n*-butyl)(*tert*-butyl)(*ortho*-trifluoromethyl-phenyl)phosphine, **8** can be prepared from the chloro phosphine and *n*-BuLi in a similar fashion, and was also characterised further as its borane complex, **10**.

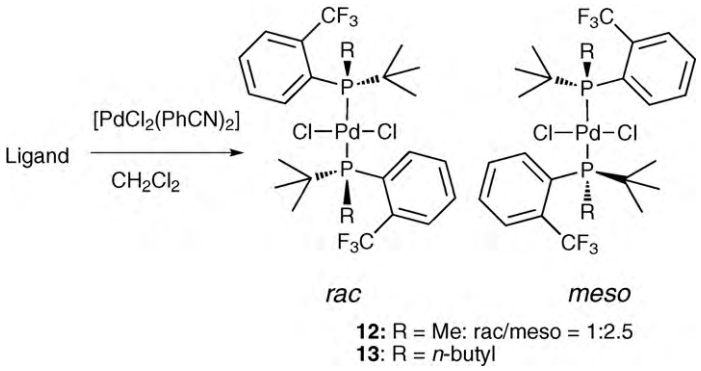
(*tert*-Butyl)-*bis*-(*ortho*-trifluoromethyl-phenyl)phosphine, **11** was simply prepared in high yield by adding an excess of *ortho*-trifluoromethylphenyl lithium to Bu^tPCl_2. The air stable solid product was isolated by recrystallisation from ethanol in 82% yield. This compound shows the expected septet at 2.6 ppm ($^4J_{P-F}$ = 51.2 Hz) in the $^{31}P\{^1H\}$ spectrum. We have not been able to prepare bis(*tert*-butyl)(*ortho*-trifluoromethyl-phenyl)phosphine by any route; surprisingly, there was no reaction between chlorophosphine **6** and *tert*-butyl lithium, or any reaction between $(Bu^t)_2PCl$ with 2-(CF_3)-C_6H_4Li with chlorophosphines recovered unchanged at the end of the reactions.

The cone angle of **11**, using the Tollman data, [6] is 217° while the cone angles of ligands **7** and **8** are 178° and 183°, respectively. Ligands **7** and **8** can therefore be considered as being more bulky than Cy_3P (170°), and quite similar to the $^tBu_3P$ ligand (cone angle = 182°), although their significantly different shape is likely to have a significant effect on the behaviour of the transition metal catalysts derived from them; subtle changes to bulky phosphines can induce very pronounced effects in organopalladium catalysis providing a further impetus for the investigations we describe here.

The reactions of **7**, **8** and **11** with the common precursor $[PdCl_2(PhCN)_2]$ were studied. Reaction of *rac*-**7** with $[PdCl_2(PhCN)_2]$ occurs quantitatively at room temperature within minutes, the product of the reaction being *trans*-$[PdCl_2(\mathbf{7})_2]$, (compound **12**) which was fully characterised (Scheme 2 and Fig. 2). Ligand **8** behaves similarly. In contrast, **11** gives no palladium complexes even after several days at 20 °C or at higher temperatures.

Although the diastereomer that crystallised was the *meso* isomer, in which both phosphine units are of the opposite configuration, the *rac* isomer, in which the phosphines are of the same configuration, is also present in solution (judging by the $^{31}P\{^1H\}$ NMR spectrum), in a 1:2.5 ratio (*rac*:*meso*).

A crystal structure of the *meso* isomer of **12** was successfully obtained and this shows that a 2:1 complex forms between the



Scheme 2. Reaction of *rac*-**7** and *rac*-**8** with $Pd(PhCN)_2Cl_2$ showing the two stereoisomers of complexes **12** and **13**.

ligand and palladium (Fig. 2). The unit cell of the complex consists of two distinct molecules with slightly different dimensions. Both molecules are made up of two phosphorous ligands that are of opposite configuration and arranged *trans* to each other. They adopt a staggered conformation about the P–Pd–P axis such that each of the substituents on phosphorous is *anti* to its counterpart when viewed along this axis. The arrangement of ligands around Pd is distorted from square planar with two acute and two obtuse Cl–Pd–P angles of 84.72(5)° for Cl *syn* P-methyl, and 95.28(5)° for Cl *syn* P–*t*-Bu (from independent molecule 1). There is some disorder in all of the trifluoromethyl groups. The distance from Pd to the closest F atoms at 2.90(1) Å (molecule 1) and 2.97(1) (molecule 2), and as such is slightly shorter than the van der Walls radii of Pd and F; it is possible that a weak electrostatic interaction locates the CF_3 groups in the vacant axial positions above the Pd square plane. The structure of complex **13** shows some similar trends, but there is no sign of a weak F–Pd interaction. The structure of **13** is shown in Fig. 3.

The performance of the Pd complexes of the monophosphines **7** and **8** was compared with triphenylphosphine (cone angle = 145°, $[PdCl_2(PPh_3)_2]$ = complex **14**) and tricyclohexylphosphine (cone angle = 170°; $[PdCl_2(PCy_3)_2]$ = complex **15**) in the hydroxycarbonylation of styrene was investigated (Scheme 3 and Table 1) [7,8].

It is well established that simple monophosphine ligands can give excellent regioselectivity and activity in this reaction, but the effects of bulky electron rich ligands such as **7** were not known.

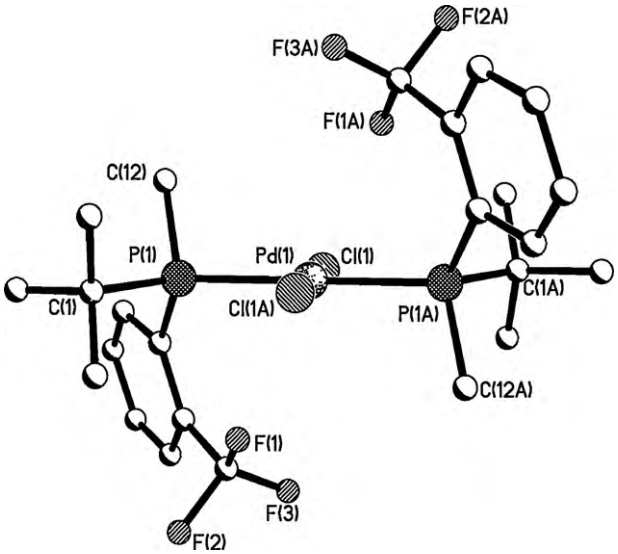


Fig. 2. X-ray crystal structure of *meso*-**12**. Hydrogens omitted for clarity.

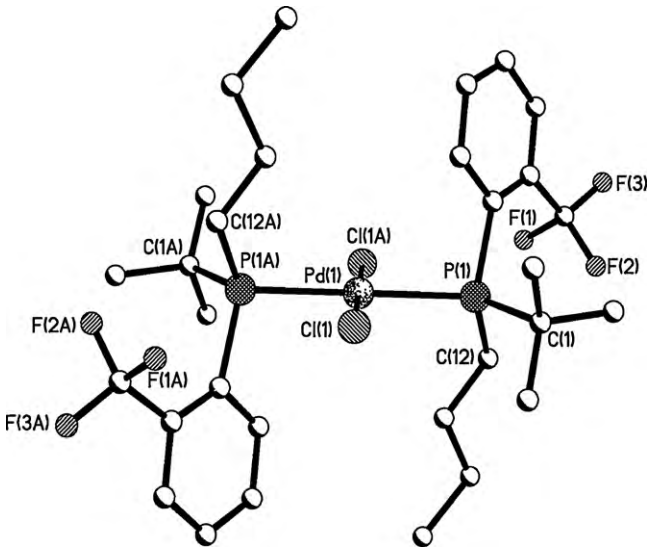
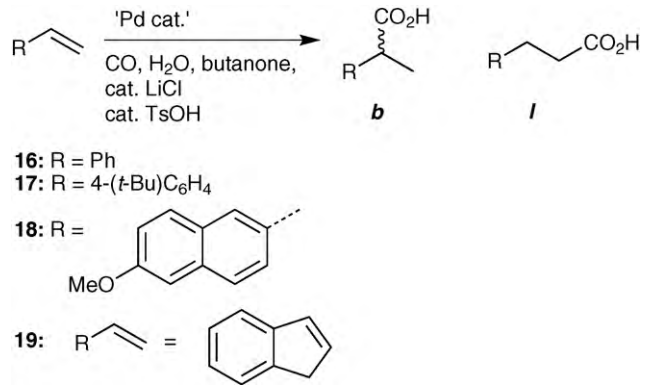


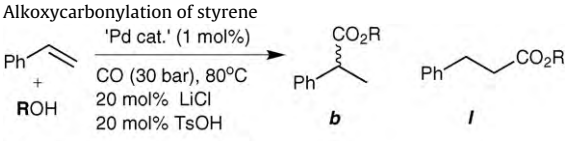
Fig. 3. X-ray crystal structure of *meso*-**13**. Hydrogens omitted for clarity.

The reactions were carried out by running the 4 catalysts in parallel at the relatively low temperature of 80 °C, since we have tended to find that temperatures below 100 °C lead to improved branched regioselectivity, albeit at the expense of activity. The results were quite striking, and somewhat unexpected. Bulky phosphines such as Cy_3P are known to give poor Pd catalysts for this reaction [4], and the tricyclohexylphosphine-based catalyst, **15** did give low yields, (Table 1, entries 2 and 6). Triphenylphosphine is known to give very good catalysts for this reaction [6d], and this is the case, since very good regioselectivity can be observed with reasonable yields using the PPh_3 catalyst, **14** (Table 1, entries 1 and 5). However, it is clear from the NMR spectra of the isolated carboxylic acid that the linear acid is a significant impurity (and cannot be separated by column chromatography). In contrast, using the Pd catalysts, **12** derived from *tert*-butyl(*ortho*-trifluoromethylphenyl)methyl phosphine, good yields that sometimes exceed those achieved with $[PdCl_2(PPh_3)_2]$ are observed, but in this case the regioselectivity is essentially perfect (Table 1, entries 3 and 7). This does have some synthetic significance in that even a few % of a difficult to separate impurity can be a serious inconvenience that could ultimately prevent the use of this clean, atom-efficient synthetic method. Furthermore, we envisaged that other substrates might have a lower in-built preference for branched regioselectivity, making this new catalyst potentially useful. Catalyst **13** although closely related to **12**, gives lower reactivity in these reactions; presumably the reac-



Scheme 3. Hydroxycarbonylation of styrene, 4-butyl styrene, 9-methoxynaphthalene and indene gives mainly branched carboxylic acids.

Table 2
Alkoxycarbonylation of styrene



(**R**OH = EtOH, Pr^{n}OH, Pr^{i}OH)

Entry[a]	Catalyst [% Pd][a]	ROH	Conv.[b] %	*b*:*l*[c]	Yield[d] %
1	14, 1.0	EtOH	58	7:1	40
2	12, 1.0	EtOH	84	43:1	58
3	14, 1.0	Pr^{n}OH	>99	7:1	73
4	12, 1.0	Pr^{n}OH	>99	73:1	73
5	14, 0.5	Pr^{i}OH	>99	10:1	92
6	12, 0.5	Pr^{i}OH	>99	64:1	84

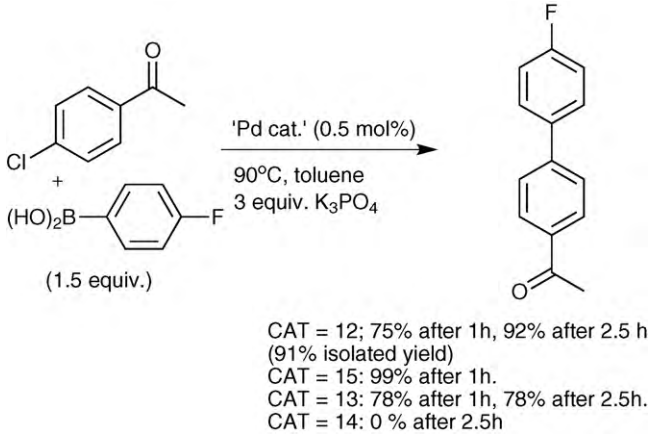
[a] Reactions carried out at 30 bar of CO, at 80 °C, 24 h, in 1.5 mL of degassed alcohol using the [$PdCl_2(L)_2$] precatalysts.
[b] ^{1}H NMR spectroscopy of reaction mixtures before work-up does not reveal any side products, hence, conversion is calculated as acids/(acids + styrene) × 100 determined.
[c] Ratio of branched/linear acid in the isolated products determined by ^{1}H NMR integration.
[d] Isolated yield of pure acids.

tion is sensitive to the cone angle of the phosphine, and **8** is just too bulky either diminishing the Pd complexes ability in one of the steps of the mechanism, or perhaps more likely giving catalysts with lower stability (Table 1, entries 4 and 8). We have not performed kinetic studies of these catalysts, since the main focus here is on understanding selectivity, but the average turnover frequencies for catalyst **12** are in the order of 15–25 mol/mol/hr at these relatively low reaction temperatures and moderate S/C ratios, and are broadly similar to triphenylphosphine-based catalysts.

Interestingly, if the LiCl additive, previously found to be important in regioselective hydroxycarbonylations is omitted [3b,6d], the selectivity for the PPh_3 catalyst is reduced significantly, but selectivity using catalyst **12** is unaffected, albeit at the expense of rate (Table 1, compare entries 9 and 10). This result is consistent with the proposal of Claver and co-workers that chloride can displace one of the phosphine ligands to give a neutral intermediate that gives enhanced selectivity [7a]; Perhaps in the case of the bulky fluorinated ligand, even tosylate anions are sufficient to displace one of the phosphines. The enhanced regioselectivity of catalyst **12** was also observed in the other vinyl arenes, **17** and **18**, with essentially perfect branched selectivity and high yield. Notably, Indene, a disubstituted alkene that to the best of our knowledge had not been investigated in hydroxycarbonylation, gave nearly perfect selectivity and high yield.

We also briefly compared catalysts **12** with PPh_3 catalyst in the alkoxycarbonylation of styrene (Table 2). These results highlight the possible significance of an inherently more regioselective catalyst, since ethoxycarbonylation gave only moderate regioselectivity to the branched ester using the PPh_3 catalyst (7:1), but this is significantly improved using catalyst **12** (43:1). Similar trends were seen in the alkoxycarbonylation using *n*-propanol or *iso*-propanol as nucleophiles.

We have successfully used complex **12** in several cross-couplings we have needed to carry out in other projects. It is an efficient catalyst that surpasses many of the plethora of Suzuki coupling catalysts, although thus far, we have not found any particularly special properties that distinguish it beyond the state-of-the-art ligands. An example that was examined and compared under controlled conditions and is relevant to this discussion is shown in Scheme 4. Coupling of 4-fluorophenylboronic acid with 4-chloroacetophenone takes place in the presence of 0.5 mol% of 12 within 2.5 h at 90 °C (T.O.F ~150 mol prod./mol cat./h). Under similar conditions, [$PdCl_2(PPh_3)_2$] returned only starting material, while [$PdCl_2(PCy_3)_2$] was an excellent catalyst for this reaction. Catalyst **13** does promote this reaction, but does not reach full conversion, perhaps suggesting that catalysts derived from this more bulky phosphine are less stable, consistent with the observations in hydroxycarbonylation.



Scheme 4. Suzuki coupling using the Pd catalysts, **12**, **13** and **15**.

4. Conclusions

Monophosphines containing *tert*-butyl groups and *ortho*-trifluoromethyl-phenyl groups are easily accessed and form *trans* complexes, after reaction with [$PdCl_2(PhCN)_2$]. The ability of Pd complex **12** to promote hydroxycarbonylation and alkoxycarbonylation with essentially perfect regioselectivity will hopefully make a small contribution towards this reaction being employed more often in organic synthesis, since high yielding, atom efficient reactions that can directly give regioisomerically and chemically pure building blocks like carboxylic acids compare favourably in terms of convenience and environmental impact relative to established methods. The methyl substituted phosphine (cone angle 178°) consistently gives more productive catalysts than the bulkier *n*-butyl substituted ligands (cone angle = 182°), while a phosphine with two *ortho*-trifluoromethylphenyl substituents does not coordinate to palladium precursors at all. The results obtained in the Suzuki reaction combined with the carbonylation data point towards catalyst stability being an issue when using the bulkier ligand, **8**. While there are many reports of the use of triphenylphosphine/Pd as a catalyst for hydroxycarbonylation and alkoxycarbonylation, the comparison made under controlled conditions here shows that this is not the optimum ligand structure in terms of regioselectivity. It is possible that the combination of a large cone angle (>170° <182°) and moderate electron donation contribute towards making ligand **7** more suited to this process compared to the PPh_3 and PCy_3 control systems. Future challenges in Pd catalysed alkene carbonylation reactions are the development of highly enantioselective systems. Initial attempts to prepare **7** in enantio-enriched form were not promising, and thus we are actively pursuing alternative approaches towards asymmetric carbonylations.

Acknowledgements

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2010.06.026.

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