

# Organometallic chemistry of bromodifluoromethyl substituted phosphines. The development of a novel nickel catalysed P–C bond forming reaction †

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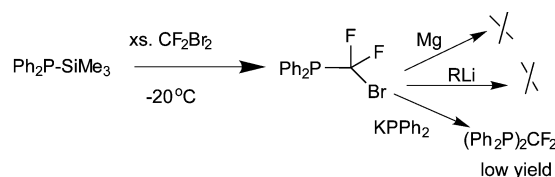
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**A new nickel catalysed coupling reaction between phosphines of type Ph<sub>2</sub>PCF<sub>2</sub>Br and silyl-substituted phosphines is reported, along with the first example of a microwave assisted phosphine synthesis.**

Phosphite, phosphonite and phosphinite ligands have many important applications in homogeneous catalysis, including hydrocyanation,<sup>1</sup> hydroformylation,<sup>2</sup> Stille and Suzuki coupling<sup>3</sup> and allylic alkylation.<sup>4</sup> Unfortunately, phosphite, phosphonite and phosphinite ligands are intolerant of moisture, acid and strong nucleophiles which limits their application in homogeneous catalysis. It is likely that the desirable catalytic properties of phosphite-derived metal complexes stems from their pronounced  $\pi$ -acceptor character. Since weak  $\sigma$ -donor/strong  $\pi$ -acceptor phosphine ligands have shown some promise in transition metal catalysis,<sup>5</sup> we are currently interested in developing electron poor phosphines that can mimic P–O type ligands.<sup>5a,6</sup> Our intention was therefore drawn to the rarely studied class of phosphines containing a P–CF<sub>2</sub>–R linkage. We report here the use of a new nickel catalysed P–C bond forming reaction to produce diphosphines of type Ph<sub>2</sub>PCF<sub>2</sub>PR<sub>2</sub>. These phosphines are analogues of the heteroatom bridged diphosphines (R<sub>2</sub>P)<sub>2</sub>O and (R<sub>2</sub>P)<sub>2</sub>NR. The latter have shown considerable promise in homogeneous catalysis.<sup>7</sup>

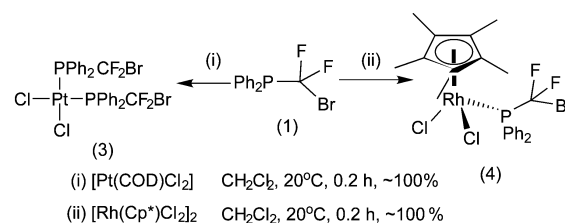
In 1991, Fild and co-workers communicated the synthesis of Ph<sub>2</sub>PCF<sub>2</sub>Br from Ph<sub>2</sub>PSiMe<sub>3</sub> and CF<sub>2</sub>Br<sub>2</sub>.<sup>8</sup> Our interest lay in using this phosphine as a precursor to phosphines of type R<sub>2</sub>PCF<sub>2</sub>R<sup>1</sup> and R<sub>2</sub>PCF<sub>2</sub>PR<sup>1,2</sup>. We have found that the reaction of Ph<sub>2</sub>PLi with CF<sub>2</sub>Br<sub>2</sub> generates (Ph<sub>2</sub>P)<sub>2</sub>CF<sub>2</sub> (**2**) in low to moderate yield and we experienced even more difficulty in functionalising isolated Ph<sub>2</sub>PCF<sub>2</sub>Br.<sup>9</sup> For example, we attempted the reactions of Ph<sub>2</sub>PCF<sub>2</sub>Br with PhLi, PhZnBr, Ph<sub>2</sub>PK, CF<sub>3</sub>–SiMe<sub>3</sub>, Li-pyrrolyl and magnesium. However, all of these reactions resulted in decomposition (or no reaction), although in the case of Ph<sub>2</sub>PK, a mixture that clearly contained (Ph<sub>2</sub>P)<sub>2</sub>CF<sub>2</sub> as a minor product was obtained [ $\delta_p = 5.5$ , t,  $^2J_{p-f} = 73$  Hz;  $\delta_f = -95$ , t,  $^2J_{f-p} = 73$  Hz]. The chemistry of halodifluoromethylene-substituted compounds with reactive organometallics is often complicated by the formation of carbene species or surprisingly low electrophilicity. We elected to study the organometallic chemistry of Ph<sub>2</sub>PCF<sub>2</sub>Br with a view to facilitating new P–C and C–C bond forming reactions.

As a starting point, the ability of Ph<sub>2</sub>PCF<sub>2</sub>Br to act as a ligand to metals in positive oxidation states was confirmed.<sup>9,10</sup> Ph<sub>2</sub>PCF<sub>2</sub>–



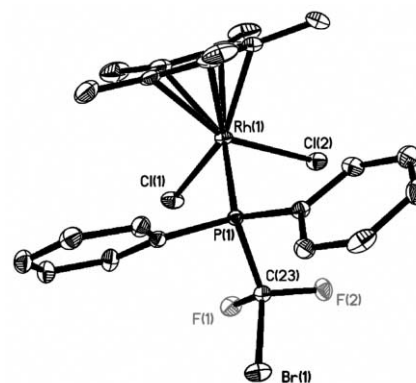
**Scheme 1** Synthesis and reactivity of Ph<sub>2</sub>PCF<sub>2</sub>Br.

Br readily reacts with [PtCl<sub>2</sub>(COD)] to yield the expected complex *cis*-[PtCl<sub>2</sub>( $\kappa^1$ -Ph<sub>2</sub>PCF<sub>2</sub>Br)<sub>2</sub>] (**3**). Ph<sub>2</sub>PCF<sub>2</sub>Br reacts with the Rh(III) precursor [Rh(Cp\*)Cl<sub>2</sub>]<sub>2</sub> as a monodentate ligand to give complex, **4**. These experiments confirm that the CF<sub>2</sub>Br group does not inhibit the co-ordination of this phosphine to transition metals. This is in contrast to other fluorinated phosphines studied in these laboratories that do not react or require extended reaction times to produce the expected Rh(III) or Pt(II) complexes.



**Scheme 2** Reaction of Ph<sub>2</sub>PCF<sub>2</sub>Br with Rh(III) and Pt(II) complexes.

Recrystallisation of **4** from CH<sub>2</sub>Cl<sub>2</sub>/hexane gave crystals suitable for an X-ray crystal structure determination (Fig. 1).<sup>11</sup> The crystal structure shows that **4** has the expected *pseudo*-octahedral piano-stool geometry in which ligand **1** adopts monodentate co-ordination. This structure was of additional interest to us as it allowed a direct comparison to the related structure, [RhCp\*Cl<sub>2</sub>( $\kappa^1$ -Ph<sub>2</sub>PC(O)CH<sub>3</sub>)], that we have reported recently.<sup>6</sup> This structure showed that the P–C bond to the acetyl group was amongst the longest reported for a phosphine metal complex [P–C(O)CH<sub>3</sub> = 1.917(2) Å]. This was rationalised as arising in part from electrostatic interactions between the electropositive acyl carbon and co-ordinated phosphorus atom. We therefore predicted, and observed a similarly long P–C bond length within complex **4** [P(1)–C(23) = 1.902 Å].



**Fig. 1** X-ray structure of complex **4**. Important bond lengths (Å): Rh(1)–P(1) 2.3206(14); P–C(Ph) 1.814(5), 1.821(6).

The reactions of Ph<sub>2</sub>PCF<sub>2</sub>Br with low-valent transition metal complexes such as [Pd(PCy<sub>3</sub>)<sub>2</sub>], Ni(COD)<sub>2</sub>/L and Pt(NBD)<sub>3</sub>/L gave mixtures of species that were generally shortlived at room

† Electronic supplementary information (ESI) available: Selected spectroscopic data and procedures, and crystal structure information for *trans*-[Pd(Cy<sub>3</sub>P)<sub>2</sub>Br<sub>2</sub>]. See <http://www.rsc.org/suppdata/dt/b3/b311799e/>

**Table 1** Nickel catalysed coupling reaction of Ph<sub>2</sub>PCF<sub>2</sub>Br<sup>a</sup> with nucleophiles

Entry	Nucleophile	t/h	T/°C	(1) %	(6) %	Ph <sub>2</sub> PCF <sub>2</sub> PR <sub>2</sub> %, [catalyst]
1	Ph <sub>2</sub> PSiMe <sub>3</sub>	24	110	~20	~30	~40 [no cat.]
2	Ph <sub>2</sub> PSiMe <sub>3</sub>	20	110	0	25	65 [cat = 5]
3 <sup>c</sup>	Ph <sub>2</sub> PSiMe <sub>3</sub>	40	85	0	24	76 [cat = 5]
4 <sup>b</sup>	Ph <sub>2</sub> PSiMe <sub>3</sub>	18	80	0	5	95 [cat = 5]
5 <sup>b</sup>	Ph <sub>2</sub> PSiMe <sub>3</sub>	18	80	25	30	45 [Ni(dppe)Cl <sub>2</sub> ]
6 <sup>b</sup>	Ph <sub>2</sub> PSiMe <sub>3</sub>	18	80	0	10	90 [Ni(dcyppx)COD]
7	NaBH(OMe) <sub>3</sub>	16	90	30	50	— [5]
8	NaBH(OMe) <sub>3</sub>	16	90	50	30	— [5]
9 <sup>d</sup>	NaBH(OMe) <sub>3</sub>	20	125	5	79	— [5]
10 <sup>b</sup>	<sup>1</sup> Pr <sub>2</sub> PSiCl <sub>3</sub>	40	80	25	41	34 (R = <sup>1</sup> Pr) [5]
11 <sup>b,e</sup>	R' <sub>2</sub> PSiMe <sub>3</sub> <sup>e</sup>	40	75	0	38	62 [5] R = NCCH <sub>2</sub> CH <sub>2</sub>
12 <sup>b</sup>	Ph <sub>2</sub> PSiMe <sub>3</sub>	0.5	~165	0	8	92 [5]

<sup>a</sup> The reactions were carried out in toluene solvent using 1.2 equiv. nucleophile and 3 mol% [Ni(dippf)Cl<sub>2</sub>] unless stated. Product yields based on Ph<sub>2</sub>PCF<sub>2</sub>Br and determined by <sup>19</sup>F NMR. Product identity was further confirmed by <sup>31</sup>P NMR and FAB mass spectra. Unidentified side products account for any remaining mass balance. <sup>b</sup> Reactions carried out in the dark, acetonitrile used as solvent. <sup>c</sup> 1.8 Equiv. of Ph<sub>2</sub>PSiMe<sub>3</sub> used. <sup>d</sup> 2 Equiv. of NaBH(OMe)<sub>3</sub> used. <sup>e</sup> 2 Equiv. of (NCCH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>PSiMe<sub>3</sub> used as nucleophile.

temperature and require further study. For example, adding [Pd(PCy<sub>3</sub>)<sub>2</sub>] to a solution of Ph<sub>2</sub>PCF<sub>2</sub>Br generates, after one hour, [*trans*-PdBr<sub>2</sub>(PCy<sub>3</sub>)<sub>2</sub>] as the major product ( $\delta_p = 26$  ppm, also characterised by X-ray diffraction).<sup>9</sup> These experiments suggest that the C–Br functionality is cleaved in the presence of low-valent transition metal complexes.

The use of a transition metal catalyst to facilitate C–Br cleavage presented itself as an intriguing possibility. We elected to develop a nickel catalysed P–C bond forming reaction between R<sub>2</sub>PCF<sub>2</sub>Br and R<sub>2</sub>PSiMe<sub>3</sub>. Nickel complexes undergo facile oxidative addition and reductive elimination and therefore should make ideal catalysts if the reaction were to proceed through a cross-coupling reaction. The novel catalyst [NiCl<sub>2</sub>(dippf)] (**5**) (dippf = bis-diisopropylphosphinoferrrocene) was therefore prepared as we felt that it should be particularly reactive due to its high basicity, bulkiness and wide bite angle.

The reaction of Ph<sub>2</sub>PCF<sub>2</sub>Br with Ph<sub>2</sub>PSiMe<sub>3</sub> in the absence of catalyst gives a low yield of (Ph<sub>2</sub>P)<sub>2</sub>CF<sub>2</sub> (20–40%) even after extended refluxing in xylene. However, in the presence of [NiCl<sub>2</sub>(dippf)] (3 mol%), improved yields up to 95% of the desired product were obtained (Table 1, entries 2–4). In contrast to the uncatalysed reaction, conversion of Ph<sub>2</sub>PCF<sub>2</sub>Br was 100%. The main side product from these reactions was Ph<sub>2</sub>PCF<sub>2</sub>H (**6**) ( $\delta_p = -10.2$ ,  $t, {}^2J_{P-F} = 120$  Hz,  $\delta_F = -117$ ,  ${}^2J_{F-P} = 120$  Hz,  ${}^2J_{F-H} = 52$  Hz). The analogous compounds (RO)<sub>2</sub>P(O)CF<sub>2</sub>H have been isolated as the major product in the reaction of (RO)<sub>2</sub>P(O)CF<sub>2</sub>-Br with nucleophiles.<sup>12</sup> Our results seem to imply that this side-product is minimised in the absence of sunlight. When [NiCl<sub>2</sub>(dppe)] was used as catalyst under identical conditions, significantly lower yields of **2** were observed (compare Table 1, entries 4 and 5). This is another example where the use of a bulky, electron rich phosphine promotes an otherwise difficult transition metal catalysed coupling reaction.

The reaction seems likely to proceed by oxidative addition of Ph<sub>2</sub>PCF<sub>2</sub>Br to the Ni(0) centre, followed by transmetalation of the nucleophilic reagent and reductive elimination of the desired products. Consistent with this mechanism is the finding that the nickel(0) bis-dicyclohexylphosphino-xylene (dcyppx) complex [Ni(COD)(dcyppx)]<sup>13</sup> is also a good catalyst for this reaction. The reduction of [Ni(L<sub>2</sub>)Cl<sub>2</sub>] by phosphines is well precedented, and in this case we believe that the formation of (Ph<sub>2</sub>P)<sub>2</sub> (<sup>31</sup>P NMR:  $\delta \sim -15$  ppm) from Ph<sub>2</sub>PSiMe<sub>3</sub> delivers the active Ni(0) species. However, we cannot rule out a radical based mechanism as halofluorocarbons frequently react by one-electron pathways. Ph<sub>2</sub>PCF<sub>2</sub>H can be prepared as the major product by the reaction

of Ph<sub>2</sub>PCF<sub>2</sub>Br with NaBH(OMe)<sub>3</sub> as nucleophilic reagent (Table 1, entries 7–9). Other nucleophiles studied include <sup>1</sup>Pr<sub>2</sub>PSiCl<sub>3</sub> and (NCCH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>P–SiMe<sub>3</sub>. A 33% conversion to Ph<sub>2</sub>PCF<sub>2</sub>P<sup>1</sup>Pr<sub>2</sub> and 62% conversion to Ph<sub>2</sub>PCF<sub>2</sub>P(CH<sub>2</sub>CH<sub>2</sub>CN)<sub>2</sub> were observed under unoptimised conditions. Thus this new reaction can be used in the synthesis of unsymmetrical diphosphines.

Finally, 30 min of controlled microwave irradiation (80 W, MeCN, sealed tube, *ca.* 160 °C) allows the coupling of Ph<sub>2</sub>PCF<sub>2</sub>-Br and Ph<sub>2</sub>PSiMe<sub>3</sub> to take place in near quantitative yield with minimal formation of the side product Ph<sub>2</sub>PCF<sub>2</sub>H. This is, to the best of our knowledge, the first example of a microwave assisted phosphine synthesis. The microwave assisted reaction was also applied to the direct Ni catalysed reaction between <sup>1</sup>Pr<sub>2</sub>PSiCl<sub>3</sub> and CF<sub>2</sub>Br<sub>2</sub> to yield the novel bulky diphosphine (<sup>1</sup>Pr<sub>2</sub>P)<sub>2</sub>CF<sub>2</sub> in an unoptimised yield of 85% [15% <sup>1</sup>Pr<sub>2</sub>PCF<sub>2</sub>Br].

In conclusion, the reactivity of Ph<sub>2</sub>PCF<sub>2</sub>Br with transition metal complexes and nucleophilic reagents has been studied. This has allowed us to develop a novel P–C bond forming reaction to produce phosphines of type Ph<sub>2</sub>PCF<sub>2</sub>PR<sub>2</sub>. This is an unusual example of the use of transition metal catalysis in the functionalisation of organofluorine compounds and should allow the study of new CF<sub>2</sub> bridged diphosphines in catalysis.

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- See Electronic Supplementary Information (ESI)† for further details.
- All compounds reported here were characterised by multinuclear NMR and FAB mass spectroscopies. Selected analytical data: (**3**) Found: C, 33.03; H, 2.50; C<sub>27</sub>H<sub>22</sub>F<sub>4</sub>Br<sub>2</sub>Pt<sub>1</sub>P<sub>2</sub>Cl<sub>4</sub> (DCM solvate, <sup>1</sup>H NMR evidence) requires: C, 33.05; H, 2.26. (**4**) Found: C, 44.74; H, 4.07; C<sub>23</sub>H<sub>20</sub>F<sub>2</sub>Br<sub>1</sub>Cl<sub>2</sub>P<sub>1</sub>Rh<sub>1</sub> requires: C, 44.30; H, 4.05. [NiCl<sub>2</sub>(dippf)] Found: C, 47.4; H, 6.60; C<sub>22</sub>H<sub>36</sub>Fe<sub>1</sub>P<sub>2</sub> requires: C, 48.0; H, 6.96.
- Crystal data for **4**: C<sub>23</sub>H<sub>25</sub>BrCl<sub>2</sub>F<sub>2</sub>PRh. *M* = 624.12, monoclinic, space group *C2/c* (No. 15), *a* = 15.890(3), *b* = 8.3668(18), *c* = 36.119(8) Å,  $\beta$  = 92.679(4)°, *U* = 4796.7(18) Å<sup>3</sup>, *Z* = 8, *T* = 173 K, 5500 unique data, *R*<sub>1</sub> = 0.0573. CCDC reference numbers 220351 and 220352. See <http://www.rsc.org/suppdata/dt/b3/b311799e/> for crystallographic data in CIF or other electronic format.
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- Complex was generated *in situ* from [Ni(COD)<sub>2</sub>] and dcyppx.