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Novel and efficient synthesis of perfluoroalkylated arylphosphines

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Abstract

A novel, high-yield route has been developed for the synthesis of perfluoroalkylated arylphosphines, involving simple, copper-mediated coupling of haloarylphosphine oxides with perfluoroalkyl iodides followed by reduction with trichlorosilane. © 2000 Elsevier Science Ltd. All rights reserved.

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One of the current frontiers in homogeneous catalysis involves the exploration of non-traditional reaction media such as water, ionic liquids, supercritical carbon dioxide ($scCO_2$) and perfluorocarbons.[1] For catalysis in some of these solvents, modifications to ligands have to be made in order to make their metal complexes soluble. A well-established strategy for catalysis by organometallic complexes in $scCO_2$ and a fluorous phase is to modify known ligands with fluorinated groups such as perfluoroalkyls, which are known to exhibit exceptionally high solubility in these solvents.[2,3] Arylphosphines are perhaps the most widely used ligands in homogeneous catalysis.[1] Accordingly, synthetic routes have been developed for the attachment of fluorinated ponytails to these phosphines.[4–7] $PPh_{3-n}[4\text{-}C_6H_4(CH_2)_mR_f]_n$ (n=1–3, m=0, 2, R_f=perfluoroalkyl) have been prepared by bromine–lithium exchange processes between fluoroalkyl-substituted bromobenzenes and *n*BuLi at −78°C followed by metathesis with $PPh_{3-n}Cl_n$.[4–6] The disadvantages of the previous methods include that, for each fluorophosphine, the synthesis has to start with the preparation of fluoroalkylated aromatics using fluoroalkyl iodides followed by the metathesis, relies on the use of moisture-sensitive and pyrophoric organolithium reagents at low temperature and ends at relatively inefficient utilisation of the iodides, often the most expensive of all reagents involved. Herein, we describe a convenient and high-yield route to arylphosphines bearing perfluorinated ponytails based on the direct coupling of fluoroalkyl iodides with haloarylphosphine oxides.

Cross-coupling of fluoroalkyl iodides with iodoaromatic compounds to give fluoroalkyl-substituted aromatics in the presence of copper was reported by McLoughlin and Thrower more than three decades ago.[8] The reaction was later extended to include bromoaromatics.[9,10] Functional groups such as OH,

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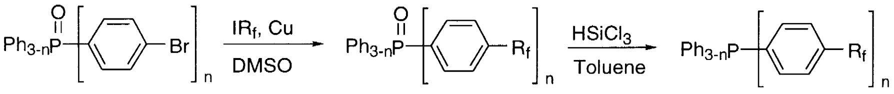
CO_2R and NH_2 in the starting aromatics are tolerated. Prompted by these early findings, we attempted the coupling of haloarylphosphine oxides with perfluoroalkyl iodides. Since these phosphine oxides are easily available starting from 1,4-dibromobenzene and phosphorus chlorides using established procedures,[11] such a reaction would offer a much simplified route to fluoroalkylated phosphines, involving just two steps, coupling and subsequent reduction (Scheme 1). To our delight, coupling of $OPPh_{n-3}(4\text{-}C_6H_4Br)_n$ (n=1–3) with IC_6F_{13} proceeded smoothly in the presence of copper powder to give the perfluorohexyl-substituted phosphine oxides $OPPh_{n-3}(4\text{-}C_6H_4C_6F_{13})_n$ in greater than 90% isolated yields (Table 1).[12] In all the cases including the coupling with IC_8F_{17}, the prefluoroalkylated phosphine oxides were obtained as crystalline solids. The obtained yields are remarkable as most previously reported coupling reactions of aryl iodides and bromides have yields lower than 70%.[8–10] The key to the success of our method is the use of oxidised phosphines. When bromoarylphosphines were employed instead of the oxides, complex mixtures were obtained under otherwise identical reaction conditions. The presence of a catalytic amount of 2,2′-bipyridine (bipy) in the reaction lowers the reaction temperature without affecting the conversion and yield. Bipy may play a role in facilitating metallation of copper by IC_6F_{13}.[8] The phosphine oxide may play a similar role, thus promoting higher yields under milder conditions. As with the coupling reactions of other haloaromatics, DMSO is the solvent of choice.[8–10] In DMF, the reaction was sluggish and less clean. The chloride analogues $OPPh_{n-3}(4\text{-}C_6H_4Cl)_n$ failed to react. A longer reaction time was required on going from $OPPh_2(C_6H_4Br)$ to $OP(4\text{-}C_6H_4Br)_3$ due to increasing substitution by the perfluorohexyl moiety and accompanied decrease in solubility of the substituted oxides in the solvent. Solubility also appears to be responsible for the slightly lower yield obtained with $OP(4\text{-}C_6H_4C_6F_{13})_3$. When the reaction was carried out in a perfluoro-1,3-dimethylcyclohexane and DMSO (5:1, vol.) mixture, the yield of $OP(4\text{-}C_6H_4C_6F_{13})_3$ increased to 95%. Solubility was even more of a problem with the longer IC_8F_{17}. Thus, when the reaction of $OP(4\text{-}C_6H_4Br)_3$ with IC_8F_{17} was performed in DMSO, a yield of only 45% was obtained. Remarkably, when performed in the perfluoro-1,3-dimethylcyclohexane and DMSO mixture, the reaction proceeded to give the substituted product in 93% isolated yield. While the coupling reactions above were performed under nitrogen, they can also be carried out in air without notable effects on yields.



Scheme 1. Synthesis of fluoroalkylated phosphines by Cu-mediated cross-coupling followed by reduction with silane. General conditions for cross-coupling: 1.0–1.1 equiv. IR_f and 2–3 equiv. copper powder (relative to bromine), 20 mol% bipy, 110–120°C, 15–72 h. General conditions for reduction: 5–15 equiv. $HSiCl_3$, 5–15 equiv. NEt_3, reflux, 6 h

The phosphines were released from the oxides by reduction with trichlorosilane.[13] The reaction was carried out by simply heating a mixture of a perfluoroalkylated phosphine oxide, trichlorosilane and triethylamine in toluene at 120°C for a few hours, affording the free phosphines in almost quantitative isolated yields (Table 2).[14] Thus, about 90% of the perfluoroalkyl reagents were effectively incorporated into the desired product. In contrast, previous methodologies led to much less efficient use of the expensive perfluoroalkyl iodides.[4–6]

In conclusion, we have developed a novel, convenient, and economical route for the synthesis of perfluoroalkylated arylphosphines useful for catalysis in $scCO_2$ and a fluorous phase. The key step of the route, requiring no special techniques to handle, comprises of the copper-mediated coupling of a haloarylphosphine oxide with a perfluoroalkyl iodide. The reaction could easily be scaled up and extended to other fluoroalkyl iodides.

Table 1
Copper-mediated cross-coupling of $OPPh_{n-3}(4\text{-}C_6H_4Br)_n$ with IR_f[a]

Solvent	n	R_f	Temp, °C	Time, h	Yield %[b]
DMSO	1	C_6F_{13}	120	15	95
DMSO	2	C_6F_{13}	120	24	94
DMSO	3	C_6F_{13}	120	36	91
DMSO	3	C_8F_{17}	120	36	45
PFDCy[c]	3	C_8F_{17}	110	72	93

[a] For typical reaction conditions, see ref. 12. [b] Isolated yield. [c] Perfluoro-1,3-dimethylcyclohexane (PFDCy) + DMSO (10:1, vol).

Table 2
Reduction of fluorophosphine oxides $OPPh_{n-3}(4\text{-}C_6H_4R_f)_n$ by trichlorosilane[a]

Solvent	n	R_f	Yield %[b]
Toluene	1	C_6F_{13}	97
Toluene	2	C_6F_{13}	98
Trifluorotoluene	3	C_6F_{13}	98
Trifluorotoluene	3	C_8F_{17}	95

[a] For typical reaction conditions, see ref. 14. All the compounds were characterised either by comparison with authentic samples or by spectroscopy and elemental analysis. [b] Isolated yield.

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References

1. *Applied Homogeneous Catalysis with Organometallic Compounds*; Cornils, B.; Herrmann, W. A., Eds.; VCH: Weinheim, 1996.
2. Jessop, P. G.; Ikariya, T.; Noyori, R. *Chem. Rev.* **1999**, *99*, 475.
3. Horváth, I. T.; Rábai, J. *Science* **1994**, *266*, 72.
4. Bhattacharyya, P.; Gudmunsen, D.; Hope, E. G.; Kemmitt, R. D. W.; Paige, D. R.; Stuart, A. M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3609.
5. Kainz, S.; Koch, D.; Baumann, W.; Leitner, W. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1628.

6. Betzemeier, B.; Knochel, P. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 2623.
7. Carroll, M. A.; Holmes, A. B. *Chem. Commun*. **1998**, 1395.
8. McLoughlin, V. C. R.; Thrower, J. *Tetrahedron* **1969**, *25*, 5921.
9. Chen, G. J.; Tamborski, C. *J. Fluorine Chem*. **1989**, *43*, 207.
10. Chen, G. J.; Chen, L. S.; Eapen, K. C. *J. Fluorine Chem*. **1993**, *65*, 59.
11. Benassi, R.; Schenetti, M. L.; Taddei, F.; Vivarelli, P.; Dembech, P. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1338.
12. A typical preparation is given for tris(4-tridecafluorohexylphenyl)phosphine oxide. A mixture of tris(4-bromophenyl)phosphine oxide (515 mg, 1.0 mmol), 1-iodoperfluorohexane (1.405 g, 3.2 mmol), copper powder (450 mg, 7.1 mmol), 2,2′-bipyridine (34 mg, 0.2 mmol) and DMSO (20 ml) was stirred at 120°C for 36 h. After cooling to room temperature, the reaction mixture was diluted with $CHCl_3$ (50 ml) and water (50 ml), filtered through a pad of Celite and washed with $CHCl_3$ (2×20 ml). The organic layer was separated, washed with 1N HCl (2×50 ml), water (2×50 ml) and brine (50 ml), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product, which upon recrystallisation from EtOH yielded the desired compound as colourless needles (1.123 g, 91%).
13. Gilheany, D. G.; Mitchell, C. M. In *The Chemistry of Organophosphorus Compounds*; Hartley, F. R., Ed.; John Wiley & Sons: Chichester, 1990; Vol. 1.
14. A typical preparation is given for tris(4-tridecafluorohexylphenyl)phosphine. A mixture of tris(4-tridecafluorohexylphenyl)phosphine oxide (2.465 g, 2.0 mmol), trichlorosilane (1.355 g, 10 mmol), triethylamine (1.518 g, 15 mmol) and toluene (20 ml) was stirred at reflux for 6 h under nitrogen. After cooling to room temperature, saturated $NaHCO_3$ aqueous solution (1 ml) was added. The mixture was stirred for 5 min at room temperature, filtered through a pad of alumina, washed with toluene (3×20 ml) and evaporated under reduced pressure to give the desired compound as white solids (2.384 g, 98%). This and all the other compounds given in Table 2 have been characterised by NMR, MS and elemental analysis or by comparison with authentic samples.