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New phosphine ligands with the OPN donor configuration

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New, functionalised phosphines with an OPN donor set which are potentially capable of square planar co-ordination were synthesized by stepwise introduction of the oxygen and nitrogen functional substituents to phosphorus. The secondary phosphines (phenyl)(tetrahydrofurfuryl)phosphine, **1**, and [2-(1,3-dioxolan-2-yl)ethyl](phenyl)phosphine, **2**, were first prepared before the introduction of the nitrogen donor substituents. The OPN phosphines (phenyl)(D^1)(D^2)phosphine {D^1 = tetrahydrofurfuryl, D^2 = 2-pyridylmethyl or pyridyl; D^1 = 2-(1,3-dioxolan-2-yl)ethyl, D^2 = 2-pyridylmethyl}, **3**–**5**, were obtained. This approach was not appropriate for the preparation of an OPN ligand with an ester functionality. Therefore the synthesis of methyl 3-[(phenyl)(2-pyridylmethyl)phosphino]propanoate, **7**, was achieved *via* a radical induced coupling of methyl acrylate to (phenyl)(2-pyridylmethyl)phosphine **6**. All new ligands, **1**–**5**, **7**, were characterised by ^{1}H, ^{13}C and ^{31}P NMR spectroscopy. The methods developed allowed the ligands to be synthesized in high yields and purity such that further purification was generally unnecessary for subsequent applications.

Introduction

In many areas of co-ordination chemistry and homogeneous catalysis there is considerable interest in phosphine ligands bearing substituents with functional groups that are physically placed to chelate to a metal.[1] The principal aim is to combine strong co-ordination *via* phosphorus with a hemilabile donor for transient stabilisation of intermediates during reaction sequences. To this end, many functionalised phosphines of the form Ph_2PR, where R bears a donor atom, have been prepared. Phosphines having two or three identical donor groups are also common and are usually easily prepared by standard methods using starting materials such as RPX_2, M_2PR or PX_3.[2,3] However, if a phosphine bearing two different donor groups is required, synthetic strategies can become significantly more complicated. Since all desired functional groups are nucleophilic and many commonly have other reactivity (*e.g.* esters, imines, amines, *etc*.) they may interfere with subsequent reactions required for the introduction of further functional substituents. Furthermore, preparation of phosphides using organolithium reagents may be poorly selective or precluded altogether if the phosphine has other reactive functions such as acidic protons, alkenes, alkynes, hydroxy, carbonyl groups, *etc*., which may compete with phosphorus metallation.[4,5] Similarly, reactions involving functionalised halogenophosphines with organolithium or Grignard reagents can also be expected to be limited by the reactivity of the functional group.

Other problems are apparent, for example Spiegel and Stelzer[6] report that the successful introduction of a 2-pyridylmethyl group to phosphorus is dependent on the metal phosphide used. Specifically, 2-chloromethylpyridine reacts cleanly with sodium phenylphosphide to give (phenyl)(2-pyridylmethyl)phosphine, but dimerisation of the pyridine unit results if the reaction is performed with lithium phenylphosphide instead. This is typical of pyridine based phosphines which are commonly plagued by side reactions and low yields.[7–12] Problems of functional group interference may be overcome in some cases by choosing an appropriate order for the introduction of the functional substituents; protection of the functional group before following substitutions; or by varying the type of reaction used for subsequent sequential substitutions at phosphorus.[11,13–18]

In the preparation of phosphines bearing two or three different substituents the selectivity of sequential substitutions is clearly important,[19–22] especially since mixtures of such phosphines having similar types of substituents also have similar physical and chemical properties often resulting in difficulties in isolation of the desired product.[23] Purification and synthetic techniques have notably improved,[2,9] and preparations involving protection of the phosphine as the borane adduct are becoming more common, especially for the synthesis of functionalised or asymmetric phosphines (*e.g.* refs. 18, 24–27).

Only a small number of phosphines exist which have both oxygen and nitrogen donor groups well placed for metal co-ordination. Phosphines which may potentially co-ordinate in a linear, tridentate manner with P, N and O atoms take one of three forms depending upon the order of the donors: PNO,[13,15,16,28–37] PON[15,16,38–40] or OPN.[16,26,41–47] The syntheses of the PNO and PON type phosphines are relatively straightforward in most cases as they require only single phosphorus substitution to yield the desired product and reported examples are typically diphenylphosphine based. Notably, only four different types of OPN phosphines have been reported. Phosphines with an OPN donor set contain two functional groups on the phosphorus atom, preparative difficulties may, at least in part, be responsible for the low number reported so far (Fig. 1).[16,26,41–47] Of these, several are unlikely to co-ordinate through O, P and N donors to a single metal centre due to the position of the donor atoms, and hence are not discussed further here.[41,45,46] Not all ligands shown in Fig. 1 were designed to form 'strong' tridentate chelates.[16,47] In most cases the ligands have been designed for homogeneous catalysis and therefore often have weaker donor arms which act as hemilabile chelates during catalysis, or to provide a chiral centre at phosphorus for purposes of asymmetric catalysis.[16,26,42,44,45]

The syntheses of oxygen and nitrogen functionalised phosphines bearing one pyridine substituent and one cyclic ether or ester substituent are described herein. Asymmetric syntheses of these phosphorus chiral ligands were not attempted. For reactions of carbon monoxide with alkenes and alkynes, pyridine and phosphine donor groups have been shown to have particular activating affects on migratory insertions of the substrates. General synthetic routes to the desired OPN ligands were sought so that changes could be made to the PN and PO chelate

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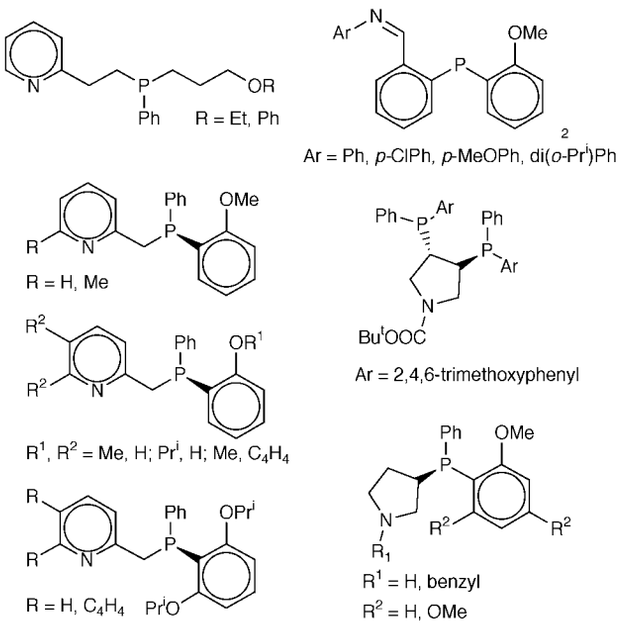


Fig. 1 Examples of known OPN phosphines which may act as linear tridentate ligands. See refs. 16, 26, 42–44, 47.

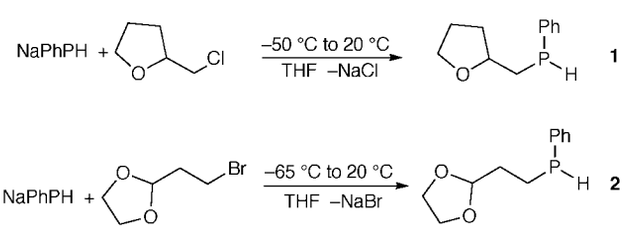
ring sizes. The oxygen donor substituent on phosphorus was included so that the ligand would have a weakly co-ordinating (hemilabile) chelate which would be available to stabilise the complex during catalysis whilst not competing too strongly with the substrates for co-ordination.

The successful synthesis of the new phosphines **3** and **4** proceeded from the previously unreported secondary phosphines (phenyl)(tetrahydrofurfuryl)phosphine **1** and [2-(1,3-dioxolan-2-yl)ethyl](phenyl)phosphine **2** in high yields and purity. A 2-pyridylmethyl functionalised phosphine ester was also prepared in high yield by alternating the order of introduction of the substituents to avoid unwanted side-reactions due to the reactivity of the ester function.

Results and discussion

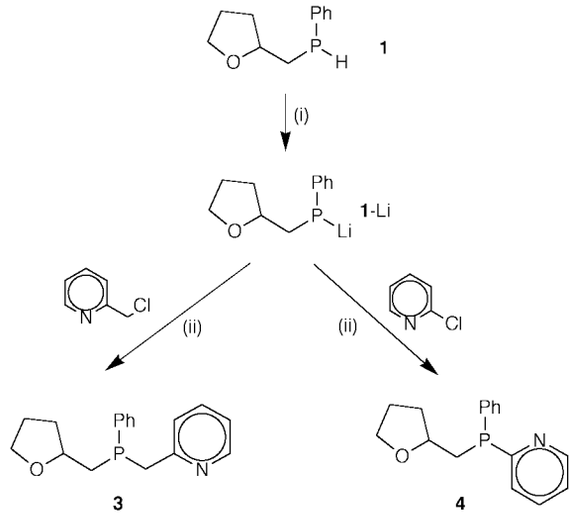
Preparation of OPN phosphines

The secondary tetrahydrofurfuryl phenylphosphine, **1**, had not been previously reported, but was prepared in virtually quantitative yield (97%) and excellent purity using a procedure based on that used by Spiegel and Stelzer[6] for (phenyl)(2-pyridylmethyl)phosphine (Scheme 1). Similarly, phosphine **2** was prepared in 100% yield (Scheme 1). Both **1** and **2** are air sensitive, colourless oils and have strong and offensive odours.



Scheme 1 Synthesis of phosphines **1** and **2**.

The lithium phosphide of compound **1** rapidly formed after addition of methyl- or *n*-butyl-lithium at −40 to −50 °C in hexanes (Scheme 2). The mixture was stirred for 30 minutes to ensure that the reaction was complete. Addition of a hexane solution of either 2-chloromethylpyridine or 2-chloropyridine results in the formation of phosphines **3** and **4**. Introducing the substituents to phosphorus in this order (N after O) proves to be an effective route, the overall isolated yield from



Scheme 2 Synthesis of phosphines **3** and **4**. (i) *n*-BuLi, hexanes, −50 °C, 30 min, − *n*-BuH; (ii) hexanes, −80 °C to 20 °C, 8 h, −LiCl.

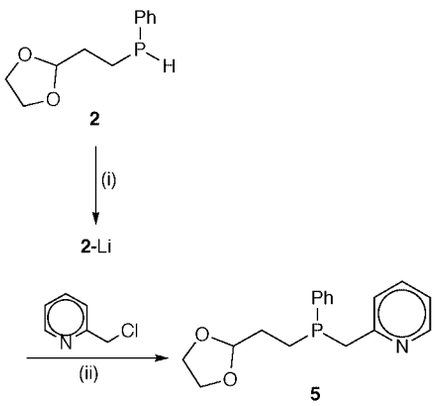
phenylphosphine being consistently over 90% in both cases (Scheme 2). It is interesting that alternating the order of introduction of the substituents is crucial since adding tetrahydrofurfuryl chloride to the sodium or lithium phosphide of **6** did not result in the formation of phosphine **3** under similar conditions. The complex product mixture did not contain even trace amounts of **3**.

The syntheses of compounds **3** and **4** were carried out initially at low temperatures (less than −80 °C) to discourage side reactions, but were allowed to warm up gradually overnight. Unexpectedly, the reaction mixture became darker compared to the light yellow suspension of **3**-Li as the addition of the alkyl halides was made. Usually, decolourisation of the phosphide commences immediately after addition of an alkyl halide, and if not it suggests that the reaction may not be successful. After approximately 24 hours, the reaction mixture ranged from light burgundy to pink for phosphine **3**, and orange to light brown for **4**. The remaining colour disappeared when deoxygenated water was added to work up the reaction mixture. Sometimes, some pink colour remained after the water was added to the reaction mixture of **3**. This appears to be due to small amounts of a bright red decomposition product of 2-chloromethylpyridine (a dimeric salt),[48] which is removed by washing the organic layer with portions of water.

The crude phosphines were isolated as viscous, air sensitive pale yellow oils in high yields and good purity. Preparations of phosphide **1**-Li using *n*-butyllithium in hexanes gave **3** and **4** in higher purity than for methyllithium in ethers. The purity is certainly adequate for further work, but the pale yellow colour of the crude phosphines indicates that there is a small amount of contamination. Hence, phosphine **3** was purified on a silica gel column with diethyl ether eluent under nitrogen to give a virtually colourless oil. It is noted however that phosphines with pyridine based substituents are often reported to be yellowish and this colour can persist after purification by vacuum distillation or recrystallisation.[8,13,26,49] Purification of **3** was also attempted by recrystallisation of its hydrochloride salt. Treatment of a diethyl ether solution of **3** with aqueous or an excess of gaseous HCl gave only the pyridinium salt. No quaternisation of phosphorus was observed (^{31}P NMR). The pyridinium salt of **3** (δ_P -14.2_{maj}, −15.6) was an oxygen sensitive solid which could not successfully be purified by recrystallisation. Similarly, treatment of **4** with an excess of aqueous HCl produced only the pyridinium salt of **4** (δ_P -16.3_{maj}, −19.0). The preference for nitrogen over phosphorus quaternisation in the presence of a controlled amount of acid or alkyl halide has been noted previously in phosphines bearing pyridine or amine substituents[41,50–56] and is due to the higher

basicity of nitrogen compared to phosphorus in these systems. However, once a nitrogen in close enough proximity has been quaternised, the inductive effect reduces the basicity of phosphorus.[50] Thus Heßler *et al.*[54] found that an excess of concentrated HCl was necessary to form the phosphonium salt of the tris(ammonium) substituted phosphine, $\{[HNMe_2\text{-}(CH_2)_2]_3P\}^{3+}\cdot 3Br^-$.

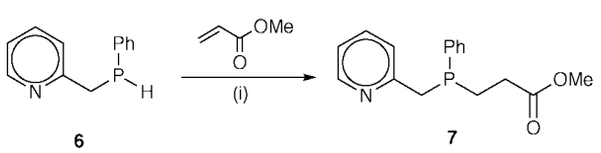
The preparation of phosphine **5** was achieved by a similar procedure, starting from **2** (Scheme 3). The formation of phosphide **2**-Li appeared to occur much more slowly than **1**-Li under the same conditions. The lithiation of **2** would not go to completion in hexanes at room temperature even over several hours due to the low solubility of **2** and **2**-Li in hexanes; the phosphide was formed readily in THF instead. Phosphine **5** was isolated as an air sensitive, viscous, pale yellow oil in good purity and in 82% yield.



Scheme 3 Synthesis of phosphine 5. (i) *n*-BuLi, THF, −80 to 0 °C, 30 min, −*n*-BuH; (ii) hexanes, −30 to 20 °C, 1.5 h, −LiCl.

The synthetic route to phosphines **3**–**5** is satisfactory for cyclic ether substituents, but it was anticipated that it would not be suitable for the preparation of analogous phosphines bearing carbonyl oxygen donor substituents. The higher reactivity of a carbonyl group with nucleophiles such as organolithium reagents may result in side reactions occurring. Therefore, in attempting to make a carbonyl containing OPN ligand, the syntheses were designed so that the carbonyl substituent was introduced last.

An appropriate route is by the addition of an alkene to a secondary phosphine which has been used with success in several relevant studies.[11,41,42] The reaction of compound **6** and methyl acrylate was attempted in the presence of a catalytic amount of azobis(isobutyronitrile) (AIBN) to initiate the radical catalysed hydrophosphination of the alkene (Scheme 4).



Scheme 4 Synthesis of phosphine **7**. (i) AIBN, toluene, reflux.

This procedure gave good yields of phosphine **7**, as an air sensitive viscous yellow oil which could not be distilled without decomposition. When this reaction was performed under Michael addition conditions[41] none of the desired phosphine **7** was produced. Instead, the major product (or products) appear to be secondary phosphines which result from addition of methacrylate at the pyridylmethylene position [$\delta_P(CDCl_3)$ −44.1, −45.4; *cf.* phosphine **6**, δ_P ($CDCl_3$) −46.6].

To purify phosphine **7** further several methods were attempted. Preparation of the pyridinium hydrochloride salt appeared to result in degradation of the ester group. After neutralisation of the HCl salt with deoxygenated aqueous $NaHCO_3$ solution, the ^{31}P NMR spectrum showed several new peaks at around δ −14.5 in CD_3CN, which suggests that the substituents had perhaps been altered at a position remote from the phosphorus atom, most probably by hydrolysis of the ester group. Purification of phosphine **7** *via* formation of a borane was not attempted since boranes are likely to interact with all three functional groups (some phosphine–borane complexes are known to catalyse the reduction of ketones and esters[57]) and the liberation of the free phosphine may also lead to complications.[57–59] Phosphine **7** was readily purified however by dissolution of the crude product in solvents in which the impurities had low solubility and removing these *via* filtration.

Table 1 ^{31}P NMR data for phosphines **1**–**5**, **7** recorded in $CDCl_3$ unless stated

Phosphine	^{31}P NMR δ ($^1J_{PH}$/Hz)
1	−65.7 (212)
2	−51.9[a]
3	-26.7_{maj}, -27.8_{min}
4	−21.2, −21.3
5	−19.8
7	−20.5, −14.5,[b] −20.5[c]

[a] Spectrum shows complex PH coupling, unable to determine $^1J_{PH}$. [b] In CD_3CN. [c] In toluene.

Characterisation of OPN phosphines

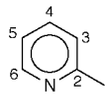
All the phosphines prepared, **1**–**5**, **7**, are chiral at phosphorus and **1**, **3** and **4** are also chiral at carbon. All were characterised by ^1H, ^{13}C, ^{31}P NMR and mass spectroscopy, but their oxygen sensitivity prevented the acquisition of accurate microanalyses. The ^{31}P NMR spectra of **3** and **4** have two peaks due to the presence of two diastereomeric pairs (Table 1). In the case of **3** the two groups of diastereomers are present in a 4:3 ratio whereas for **4** the ratio is approximately 1:1. A mixture of diastereomers is predicted for the secondary phosphine **1** as well, although no chemical shift difference was observed in the ^{31}P NMR spectrum, as has previously been noted for racemic mixtures of chiral secondary phosphines.[60]

The assignments of ^1H and ^{13}C NMR spectra were not always straightforward due to phosphorus coupling and the large number of overlapping peaks. The spectra of compounds **1**, **3** and **4** which are chiral at carbon were especially complex as a result of the magnetic inequivalence of the diastereomeric pairs as well as the usual phosphorus coupling. The use of HETCOR (heteronuclear chemical shift correlation) NMR spectroscopy was useful in determining the correct assignments. For the ^1H NMR spectra of **1**–**5**, **7**, the peaks were much more difficult to assign specifically to individual protons due the higher multiplicity of most peaks. Generally, there is little variation in ^1H and ^{13}C NMR chemical shifts and coupling constants between phosphines reported here and similar phosphines previously reported.[6,11,22,41,43,44,61,62] The data given in Tables 2–4 show the uniformity of the ^{13}C NMR chemical shifts and coupling constants, J_{CP}. All coupled peaks are doublets. The ^{13}C NMR signals for the two diastereomeric pairs are sometimes coincident, in particular the phenyl signals of phosphines **1** and **4** (Table 3), and also for the C5 pyridyl signal of **3** (Table 2). The only significant variations are observed for **4** which contains a 2-pyridyl instead of a 2-pyridylmethyl substituent and for phosphine **7** for which the spectrum was recorded in CD_3CN.

Conclusion

General and high yielding synthetic routes to six new functionalised phosphines, **1**–**5**, **7**, have been developed. The order of introduction of the functional substituents was found to have a

Table 2 ^{13}C NMR data for the pyridine substituent of phosphines **3**–**5**, **7**; $^{n}J_{PC}$/Hz in parentheses



	Phosphine	C2	C3	C4	C5	C6	PCH_2
	3[a]	157.7(4.8)	122.8(4.9)	135.4	120.2	148.4	38.6(16.9)
		157.6(4.2)	122.8(4.6)	135.3		148.5	38.5(16.8)
	4	165.4(1.9)	128.5(15.2)	135.6(5.7)	122.4	150.3	—
		165.1(2.6)	128.2(14.7)	135.5(5.6)	122.3	150.2 or 150.2(7.8)[b]	
	5	157.6(5.3)	122.8(5.3)	135.5	120.3(1.5)	148.5	38.1(17.5)
	7[c]	159.5(5.3)	124.4(4.5)	137.1	122.0(2.3)	150.1	38.4(17.5)

[a] Major diastereomeric pair signal given first. [b] Appears as two singlets or a coincident doublet. [c] In CD_3CN.

Table 3 ^{13}C NMR data for the phenyl substituent of phosphines **1**–**5**, **7**; $^{n}J_{PC}$/Hz in parentheses

Phosphine	*ipso*	*ortho*	*meta*	*para*
1	135.5(9.6)	134.1(15.0)	128.8(5.7)	128.6
	135.4(9.6)	134.0(15.2)		
2	135.0(10.5)	133.6(15.3)	128.4(5.7)	128.2
3[a]	137.1(15.9)	132.1(20.1)	127.7(6.9)	128.5
	136.7(16.4)	132.0(19.7)	127.7(7.0)	128.4
4	137.7(15.4)	134.3(21.0)	128.9(7.5)	129.7
	137.6(15.4)	134.2(21.2)		129.6
5	136.7(16.7)	131.9(19.0)	127.8(6.1)	128.5
7[b]	138.4(17.5)	133.5(19.0)	129.5(6.8)	130.2

[a] Major diastereomeric pair listed first. [b] In CD_3CN.

large impact on the success of the reaction and also the purity of the final product. Phosphine **7** contains an ester function which was introduced *via* a radical initiated addition reaction of a secondary phosphine to an acrylate. All phosphines **1**–**5**, **7** have good purity as isolated from the reaction mixture and may be used without further purification. Very few phosphines which may be capable of square planar tridentate OPN co-ordination have previously been reported. Phosphines **3**–**5**, **7** are also noteworthy as relatively uncommon examples of trisubstituted phosphines bearing two different functional substituents with any type of functional group. Functionalised phosphines and tridentate chelating phosphines are sought after for their interesting co-ordination properties and potential for use in homogeneous catalysis. Studies of the co-ordination chemistry and catalysis of **3**–**5** and **7** with Pd^{II} have shown that they have unusual and interesting behaviour compared to related ligands with fewer functionalised substituents. These studies will be described in a forthcoming paper.[63]

Experimental

All phosphine preparations were carried out using Schlenk/vacuum line techniques in an efficient fumehood. All secondary and tertiary phosphines should be treated as potentially highly toxic and were handled accordingly; the secondary (and to a lesser extent the tertiary) phosphines described in this paper are all air-sensitive, noxious, foul smelling liquids or oils. NMR spectra were recorded on the following spectrometers: a JEOL FX90Q operating at 36.23 MHz (^{31}P), a Bruker WM360 operating at 145.784 MHz (^{31}P), a Bruker DPX400 operating at 400.13 (^{1}H) or 100.486 (^{13}C) MHz, a Varian Unity Inova 400 WB operating at 161.926 or 161.807 (^{31}P), 100.587 or 100.509 (^{13}C), 399.716 (^{1}H) MHz or a Varian Gemini-200 operating at 50.289 (^{13}C), 199.98 (^{1}H) MHz. The ^{1}H and ^{13}C chemical shifts (δ) are quoted in ppm relative to internal $SiMe_4$ or residual solvent and ^{31}P chemical shifts in ppm relative to 85% external H_3PO_4 (δ 0). Coupling constants (J) are listed after the chemical shifts in respective order. Those other than simple HH couplings are denoted by subscripts. Atmospheric pressure chemical ionisation mass spectrometry (APCI) measurements were made on a Finnigan "LCQ" spectrometer. The sample was added to a 40% methanol, 60% acetic acid (5% in water) solution at a rate of 0.3 cm^3 min^{-1} *via* a 5×10^{-3} cm^3 loop injection, with detection of *m*/*z* between 150 and 600. Electron ionisation (EI) mass spectroscopy measurements were recorded on either an AEI MS902 or a VG7070E instrument operating at 70 eV.

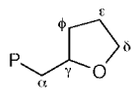
Preparation of starting materials

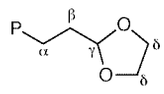
All reagents were obtained from Aldrich Chemical Company and used as received unless otherwise stated. Solvents were dried and deoxygenated by standard methods.[64] Phenylphosphine was prepared in high yield by $LiAlH_4$ reduction of $PhPCl_2$ in ether, and purified by vacuum distillation.[65] (Phenyl)(2-pyridylmethyl)phosphine **6** was prepared in >80% yields by reaction of 2-chloromethylpyridine and sodium phenylphosphide using the method of Spiegel and Stelzer.[6] However, rather than filtering the reaction mixture to remove NaCl, the organic phase was washed three times with deoxygenated water, dried over deoxygenated $MgSO_4$, and the solvent evaporated. The product is obtained in high purity by this method and further purification was unnecessary. 2-(2-Bromoethyl)-1,3-dioxolane was dried over 5A molecular sieves, vacuum distilled and stored under nitrogen in the dark. 2-Chloromethylpyridine was released from the HCl salt by neutralisation with $NaHCO_{3(aq)}$, then extracted into dichloromethane, dried over $MgSO_4$ and the solvent removed by evaporation *in vacuo*. 2-Chloropyridine was dried by stirring over KOH pellets before being distilled under nitrogen. Methyl acrylate was purified by the procedure given in Armarego and Perrin,[64] and stored in the dark under nitrogen at −20 °C. Tetrahydrofurfuryl chloride was dried over 5A molecular sieves and freeze–thaw degassed.

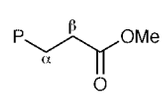
Phosphine syntheses

(Phenyl)(tetrahydrofurfuryl)phosphine 1. This synthesis is based on the method used by Spiegel and Stelzer[6] for the preparation of (phenyl)(2-pyridylmethyl)phosphine **6**. The compound $PhPH_2$ (10 cm^3, 10 g, 91 mmol) was added to a stirred suspension of sodium wire pieces (3.58 g, 156 mmol) in THF (180 cm^3) and refluxed for 5 hours. Tetrahydrofurfuryl chloride (11.10 g, 92 mmol) was dissolved in THF (130 cm^3) and cooled to −50 °C. After cooling to room temperature, the orange PhPHNa suspension was syringed into the tetrahydrofurfuryl chloride solution slowly over 15 minutes. The reaction mixture was left to stir (8 h), after which time it had decolourised completely. The solvent was reduced to *ca*. 100 cm^3 and hexanes (140 cm^3) were added. The mixture was washed with degassed water (3×30 cm^3) and the organic layer dried over degassed $MgSO_4$. Removal of the $MgSO_4$ and solvent left a clear, colourless oil (17.2 g, 97%) determined to be the pure secondary

Table 4 ^{13}C NMR data for the O donor substituent of phosphines **1**–**5**, **7**







Phosphine	α	β	γ	δ		Other
1	30.5(10.3)	—	78.9(13.9)	68.3	ε	26.3
	30.3(9.7)		78.0(15.5)	68.1		26.2
					φ	32.6(4.6)
						32.5(4.9)
2	17.2(11.0)	32.6(6.9)	104.3(9.1)	65.3		
3[a]	33.8(15.1)	—	76.6(18.4)	67.0	ε	25.2
	33.1(15.5)		76.2(16.4)			25.2
					φ	32.1(6.6)
						31.7(6.9)
4	34.7(16.2)	—	77.4(18.4)	68.1	ε	26.3
	34.6(16.3)		77.2(18.1)	68.0		26.2
					φ	32.9(6.7)
						32.8(7.1)
5	20.4(13.7)	29.5(15.2)	103.8(13.6)	64.3		
7[b]	23.2(14.4)	31.1(17.5)	—	—	OMe	52.2
					C=O	174.3(12.2)

[a] Major diastereomeric pair listed first. [b] In CD_3CN.

phosphine by NMR spectroscopy. δ_H(400 MHz; $CDCl_3$) 7.4 (2 H, m, Ph), 7.2 (3 H, m, Ph), 4.16, 4.11 (1 H, 2dt partly obscured, J_{HP} = 214, 208, J_{HH} = 7.3, 7.5 Hz, PH), 3.8–3.6 (3 H, m, CH_2OCH), 2.2–1.6, 1.4 (6 H, m, $CH_2CH_2CHCH_2P$); δ_P(36 MHz; $CDCl_3$) −65.7 (d, J_{HP} = 212 Hz) {oxide: 21.2, 20.0}; *m*/*z* (EI) 194 (M^+, 7), 85 ($OC_4H_7CH_2^+$, 100), 77 (Ph^+, 82) and 71 ($(THF - H)^+$, 30%).

[2-(1,3-Dioxolan-2-yl)ethyl](phenyl)phosphine 2. The compound $PhPH_2$ (2.0 cm^3, 2.0 g, 18.2 mmol) was added to a stirred suspension of sodium wire pieces (0.55 g, 23.9 mmol) in THF (50 cm^3) and refluxed for 5 hours. 2-(2-bromoethyl)-1,3-dioxolane (3.38 g, 18.7 mmol) was dissolved in THF (80 cm^3) and cooled to −65 °C. The orange PhPHNa suspension was allowed to cool to room temperature before being added dropwise *via* syringe to the 2-(2-bromo)ethyl-1,3-dioxolane solution over 15 minutes. The reaction mixture decolourised immediately and was left to stir and warm up (8 h). The solvent was reduced to *ca.* 50 cm^3 and hexanes (70 cm^3) were added. The mixture was washed with degassed water (25 cm^3, then 2 × 10 cm^3) and the organic layer dried over degassed $MgSO_4$. Removal of the $MgSO_4$ and solvent left a clear, colourless oil (3.81 g, 100%) determined to be the pure secondary phosphine by NMR spectroscopy. δ_H(400 MHz; $CDCl_3$) 7.33 (2 H, m, Ph), 7.15 (3 H, m, Ph), 4.71 (1 H, t, *J* = 4.3 Hz, OCHO), ≈4.0 (1 H, br d, high field peak obscured by multiplet at 3.71, PH), 3.71 (4 H, m, OCH_2CH_2O), 1.8–1.6 (4 H, m, PCH_2CH_2CH); δ_P(146 MHz; $CDCl_3$) −51.9 {oxide: 27.8}; *m*/*z* (EI) 211 (MH^+, 80), 209 ($\{M - H\}^+$, 60), 181 ($\{MH - C_2H_6\}^+$, 83), 109 ($PPhH^+$, 58), 87 ($\{CH_2CH(OCH_2CH_2O)\}^+$, 59) and 73 ($\{CH(OCH_2CH_2O)\}^+$, 100%).

(Phenyl)(2-pyridylmethyl)(tetrahydrofurfuryl)phosphine 3. (Phenyl)(tetrahydrofurfuryl)phosphine **1** (4.66 g, 24.0 mmol) was dissolved in hexanes (200 cm^3) and cooled to −50 °C and a solution of *n*-BuLi at room temperature (14 cm^3, 1.72 M in hexanes, 24 mmol) added. This immediately resulted in a lemon yellow suspension which was left to stir at < −40 °C for 30 minutes. A solution of 2-chloromethylpyridine (3.06 g, 24.0 mmol) in hexanes (30 cm^3) was added slowly to the phosphide suspension which was held at below −80 °C. Addition of the 2-chloromethylpyridine caused the suspension to become a darker yellow. Following the addition, the mixture was allowed to warm to room temperature with stirring (8 h); the pink-yellow suspension was washed with degassed water (40 cm^3 and then 2 × 20 cm^3). The resulting clear yellow solution was dried over degassed $MgSO_4$, filtered through Celite® and evaporated to leave a clear, pale yellow oil (6.37 g, 93%). The product was obtained in satisfactory purity as indicated by NMR spectroscopy and used without further purification. If necessary, it can be purified under nitrogen on a silica gel column with ether as eluent to give a colourless oil. δ_H(400 MHz; $CDCl_3$) 8.39 (1 H, m, C_5H_4N), 7.4–7.2 (6 H, m, Ph + C_5H_4N), 6.84 (1 H, pseudo t, C_5H_4N), 6.42 (1 H, 2 pseudo d, C_5H_4N), 3.9–3.5 (3 H, m, $CHOCH_2$), 3.25 (2 H, m, $PCH_2C_5H_4N$), 2.1 (1 H, m, $PCH_aHC_4H_7O$), 1.9–1.3 (5 H, m, $PCH_bHC_4H_7O + CH_2CH_2CH$); δ_P(36 MHz; $CDCl_3$) -26.7_{maj}, −27.8, {oxide: 33.1, 32.8_{maj}}; *m*/*z* (EI) 285 (M^+, 50), 200 ($PPh(CH_2C_5H_4N)^+$, 94), 193 ($PPh(CH_2C_4H_7O)^+$, 100), 123 ($P(CH_2C_5H_4N)^+$, 70), 108 (PPh^+, 65), 92 ($CH_2C_5H_4N^+$, 55), 77 (Ph^+, 93) and 71 ($(THF - H)^+$, 85%).

(Phenyl)(2-pyridyl)(tetrahydrofurfuryl)phosphine 4. The procedure adopted for compound **4** was the same as that described for **3** but using **1** (4.33 g, 22.3 mmol) and 2-chloropyridine (2.57 g, 22.6 mmol) rather than 2-chloromethylpyridine, yielding a yellow oil (5.72 g, 95%). The purity of the product is adequate for most uses, but it can be further purified as described for **3** above. δ_H(400 MHz; $CDCl_3$) (Note: H* = OCH) 8.58 (1 H, d, *J* = 7.74, C6 of C_5H_4N), 7.6–7.2 (8 H, m, Ph + C_5H_4N), 3.85 (1 H, m, OCH), 3.78 (1 H, m, $OCHH$), 3.61, 3.59 (1 H, 2q, *J* = 8.1, 8.2, $OCHH$), 2.72, 2.60 (1 H, 2dd, J_{HbH*} = 6.6, 7.6, J_{HaHb} = 13.5, 13.5, $PCH_bHC_4H_7O$), 2.36, 2.22 (1 H, 2ddd, J_{HaP} = 2.1, 2.6, J_{HaH*} = 6.2, 6.9, J_{HaHb} = 13.5, 13.5 Hz, $PCH_aHC_4H_7O$), 2.0–1.5 (4 H, m, CH_2CH_2CH); δ_P(36 MHz; $CDCl_3$) −21.1, −21.3, {oxide: 26.9, 26.7}; (CD_3OD) −16.8, −16.9, {oxide: 31.8, 31.7}; *m*/*z* (EI) 271 (M^+, 57), 185 ($\{MH - CH_2C_4H_7O\}^+$, 98%), 109 ($PC_5H_4N^+$, 100), 108 (PPh^+, 65%), 78 ($C_5H_4N^+$, 70), 77 (Ph^+, 91) and 71 ($\{THF - H\}^+$, 52%).

[2-(1,3-Dioxolan-2-yl)ethyl](phenyl)(2-pyridylmethyl)-phosphine 5. To a solution of compound **2** (1.18 g, 5.61 mmol) in THF (130 cm^3) was added the stoichiometric amount of *n*-BuLi (3.50 cm^3, 1.6 M in hexanes, 5.61 mmol) at −80 °C. The clear golden yellow solution was left to stir for 2 hours and to warm to 0 °C. After re-cooling to −30 °C, a solution of 2-chloromethylpyridine (0.72 g, 5.64 mmol) in THF (75 cm^3) was added to the phosphide solution. The solution was left to warm to room temperature during 1.5 hours, lightening to pale yellow. The solvent was removed under vacuum and the crude residue dissolved in THF (20 cm^3) diethyl ether (20 cm^3), washed with deoxygenated water (20 cm^3 then 2 × 10 cm^3), and finally dried over $MgSO_4$. Evaporation of the solvent under

vacuum left a pale yellow oil (1.38 g, 82%). δ_H(400 MHz; $CDCl_3$) 8.48 (1 H, d, $J = 4.0$, C6 of C_5H_4N), 7.5, 7.3 (6 H, 2m, Ph + C_5H_4N), 7.10 (1 H, pseudo t, C_5H_4N), 7.96 (1 H, d, $J = 7.6$, C_5H_4N), 4.88 (1 H, t, $J = 4.6$ Hz, OCHO), 3.96–3.76 (4 H, m, OCH_2CH_2O), 3.32 (2 H, s, $PCH_2C_5H_4N$), 2.0–1.5 (4 H, m, PCH_2CH_2); δ_P(162 MHz; $CDCl_3$) −19.8, {oxide: 32.6 in THF–C_6D_6}; *m*/*z* (APCI) 318 (MOH^+, 100%).

Methyl 3-[(phenyl)(2-pyridylmethyl)phosphino]propanoate 7. Methyl acrylate (0.87 g, 10.10 mmol) and AIBN (*ca.* 0.02g) in toluene (2 cm^3) were added to (phenyl)(2-pyridylmethyl)-phosphine **6**[6] (1.71 g, 8.50 mmol) in toluene (10 cm^3). After refluxing for 30 minutes, more methyl acrylate (0.25 cm^3, 2.8 mmol) and AIBN (*ca.* 0.01 g in 1 cm^3 toluene) were added to the cooled reaction solution. This step was repeated three more times after durations of 30, 30 and 60 minutes, leaving to reflux for 60 minutes after the final addition. The toluene and excess of methyl acrylate were removed by evaporation under vacuum to leave a yellow oil of crude compound **7**. The product was purified by dissolution in acetonitrile followed by filtration to remove a small amount of insoluble material. After removal of the solvent, the phosphine was subsequently dissolved in diethyl ether and cooled to −80 °C. This led to precipitation of further amounts of impurities leaving a solution of **7** of adequate purity for further use. δ_H(400 MHz; CD_3CN) 8.48 (1 H, d, $J = 4.0$, C6 of C_5H_4N), 7.5 (3 H, m, Ph + C_5H_4N), 7.35 (3 H, m, Ph), 7.10 (1 H, pseudo t, C_5H_4N), 7.96 (1 H, d, $J = 7.6$ Hz, C_5H_4N), 3.6 (2 H, m, $PCH_2C_5H_4N$), 3.57 (3 H, s, COOMe), 2.3 (2 H, m, $CH_2C{=}O$) and 2.0 (2 H, m, PCH_2); δ_P(162 MHz; $CDCl_3$) −20.5, (CD_3CN) −14.5 {oxide: 39.1}, (toluene–C_6D_6) −20.5 {oxide: 32.1}; *m*/*z* (APCI) 304 (MOH^+, 100%).

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