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New functionalised ditertiary phosphines via phosphorus based Mannich condensation reactions

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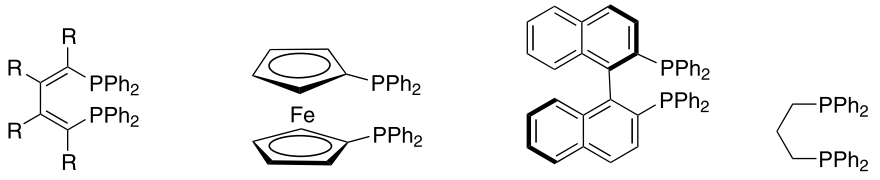
Abstract—The one-step synthesis of a family of functionalised ditertiary aminophosphines are described including the X-ray crystal structure of 4-{$(Ph_2PCH_2)_2N$}$C_6H_4CO_2H$.

Ditertiary phosphines (including chiral variants) are valuable synthetic tools widely used in coordination chemistry and homogeneous catalysis.[1] Many ditertiary phosphines have been reported to date, some pertinent examples include NUPHOS (R = Me, Ph), DPPF, (*R*)-BINAP and DPPP (Chart 1).[1,2] Of these, DPPP [DPPP = 1,3-(diphenylphosphino)propane] is the simplest and comprises a C_3-connectivity between two -PPh_2 groups.[2b] In the course of ongoing studies in our group we required a suitable ditertiary phosphine bearing backbone functionality, that would enable potential grafting onto polymeric supports. Whilst there is some literature precedence for such compounds, their functional groups[3] or syntheses[4–6] (multistep, moderate yields and/or require prior generation of a reactive phosphide intermediate) were inappropriate. Recent work by ourselves,[7,8] and others[9] have shown phosphorus based Mannich transformations to be extremely useful in accessing new 'hybrid' ligands. This synthetic procedure is versatile and offers many advantages over more classical routes, e.g. nucleophilic substitutions using primary/secondary phosphides, palladium catalysed P–C couplings and free radical additions. Herein we describe a simple high yielding one-step method for the synthesis of new functionalised ditertiary phosphines derived from cheap commercially available starting materials.

1. Results and discussion

Using a similar procedure to that recently developed for preparing novel aminocarboxylic acid tertiary phosphines,[7] reaction of two equivalents of Ph_2PCH_2OH [readily preformed from equimolar amounts of $(CH_2O)_n$ and Ph_2PH] with the appropriate stoichiometry of 4-functionalised aminoaryl precursor in refluxing methanol gave the condensed ligands 4-{$(Ph_2PCH_2)_2N$}C_6H_4X **1a**–**h** in good to high yields (Eq. (1), Table 1).[†,‡] As demonstrated by the synthesis of **1a**–**h**, this simple



NUPHOS DPPF (*R*)-BINAP DPPP

Chart 1.

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† A typical synthesis is illustrated here for **1c**. To the solids Ph_2PCH_2OH (1.007 g, 4.66 mmol) and 4-$H_2NC_6H_4CH_2CO_2H$ (0.352 g, 23.29 mmol) was added oxygen-free CH_3OH (10 ml). The yellow solution was refluxed under a nitrogen atmosphere for 4 h. The solvent was evaporated to dryness under reduced pressure to afford **1c**. Yield: 1.135 g, 89%.

‡ All new compounds gave satisfactory microanalytical and spectroscopic results.

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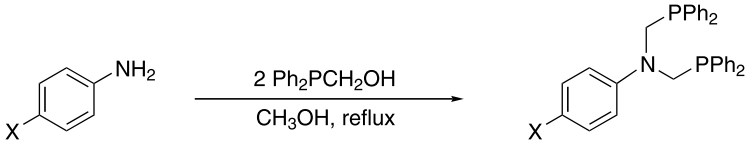
method is extremely reliable and tolerant to a range of different functional groups (CO_2H, COMe, OH, Br, I, $CH{=}CH_2$) with no significant diminishment in yield. The procedure also works well when a 4-functionalised aminobenzyl substrate is used (Eq. (2) for the synthesis of **2**) or when either 2- or 3-functionalised aminoaryls (Eq. (3)) are employed. The yields for **1**–**3** are unoptimised and in the range 50–90% with eight examples exceeding 70% (Table 1). Occasionally small amounts of 4-$\{Ph_2PCH_2N(H)\}C_6H_4X$ were detected (by NMR) indicating that reactions initially proceed through a singly substituted intermediate. The $^{31}P\{^1H\}$ NMR data (Table 1) confirm single phosphorus species at ca. δ(P) −27 ppm indicating, in all cases, that the 4-substituent exerts a negligible effect on the ^{31}P chemical shift (c.f. parent diphosphine **1a**).[10] Moreover the ^{31}P NMR resonances are some 10 ppm upfield with respect to either 4-$\{Ph_2PCH_2N(H)\}C_6H_4X$[7] or DPPP and 20 ppm upfield with respect to Ph_2PCH_2OH [δ(P) −9.9 ppm ($CDCl_3$)].[8] Compounds **1**–**3** are freely soluble in CH_2Cl_2 and THF, the acids **1b**, **1c** and **2** are also soluble in methanol but show little evidence for solubility in water or weakly basic media. Furthermore **1b**–**1h** and **2** undergo clean derivatisation (and are thereby protected) when treated with either $BH_3{\cdot}THF$, H_2O_2, S_8 or [$PdCl_2$(COD)] (COD = cycloocta-1,5-diene).

Table 1. Selected data for compounds **1**–**3**[a]

Compound	Reaction time (h)	Yield (%)	^{31}P NMR[b]	
			δ(P) (ppm)	Solvent
1a	18	79 (67)[c]	−27.2	$CDCl_3$
1b	5.5	77	−27.0	$CDCl_3/CH_3OH$
1c	4	89	−26.7	$C_6D_6/(CH_3)_2SO$
1d	48	52	−26.7	$CDCl_3$
1e	4	90	−27.5	$CDCl_3$
1f	4	74	−27.6	$CDCl_3$
1g	18	76	−27.1	$CDCl_3$
1h	4	77	−27.1	$CDCl_3$
2	4	53	−28.4	$CDCl_3$
3a	18[d]	86	−25.7	$CDCl_3$
3b	18	73	−26.8	$CDCl_3$

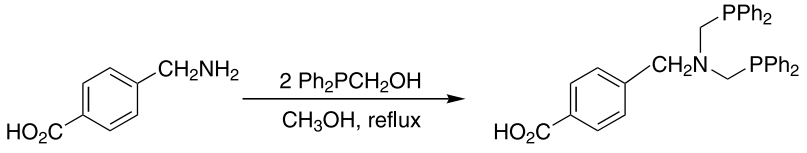
[a] Reactions performed in CH_3OH unless otherwise stated.
[b] All $^{31}P\{^1H\}$ NMR spectra recorded at 36.2 or 101.3 MHz.
[c] Taken from Ref. 10.
[d] In CH_3OH/C_7H_8.

An X-ray structure (1)[§] of **1b** confirms that the overall geometry of the ditertiary phosphine comprises 4-disubstituted $(Ph_2PCH_2)_2N$- and -CO_2H groups.[¶] The



(1)

X = H	**1a**
X = CO_2H	**1b**
X = CH_2CO_2H	**1c**
X = COMe	**1d**
X = Br	**1e**
X = I	**1f**
X = OH	**1g**
X = $CH{=}CH_2$	**1h**

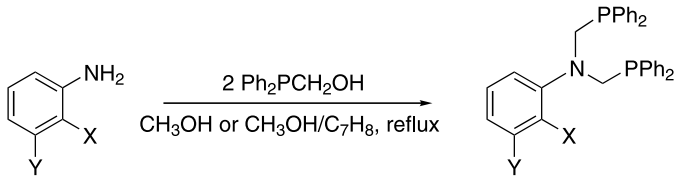


(2)

2

[§] Crystal data for **1b**: $C_{33}H_{29}NO_2P_2$, $M_w = 533.51$; triclinic, space group P-1, $a = 9.9541(7)$, $b = 11.1783(8)$, $c = 13.3554(10)$ Å, $\alpha = 70.891(2)$, $\beta = 80.274(2)$, $\gamma = 86.866(2)°$, $U = 1383.99(17)$ Å^3, $D_{calcd} = 1.280$ g cm^{-3}, λ(Mo-K$_\alpha$) = 0.71073 Å, $Z = 2$, $\mu = 0.188$ mm^{-1}, $T = 150(2)$ K, w$R_2 = 0.0932$ for all 6269 unique data, $R_1 = 0.0341$ for 5479 reflections with $F^2 > 2\sigma(F^2)$. Crystallographic data (excluding structure factors) for the structure in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 206873. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.ac.uk].

[¶] Selected bond lengths (Å) and angles (°): P(1)–C(1) 1.8827(13), P(1)–C(10) 1.8317(13), P(1)–C(16) 1.8311(13), C(1)–N(1) 1.4632(16), N(1)–C(2) 1.4633(16), C(2)–P(2) 1.8803(13), P(2)–C(22) 1.8369(14), P(2)–C(28) 1.8293(14), C(9)–O(1) 1.3208(16), C(9)–O(2) 1.2273(16). C(1)–P(1)–C(10) 97.95(6), C(1)–P(1)–C(16) 101.73(6), C(10)–P(1)–C(16) 102.39(6), P(1)–C(1)–N(1) 112.21(9), C(1)–N(1)–C(2) 115.42(10), N(1)–C(2)–P(2) 113.11(9), C(2)–P(2)–C(22) 99.07(6), C(2)–P(2)–C(28) 100.68(6), C(22)–P(2)–C(28) 102.32(6).



(3)

X = OH, Y = H **3a**
X = H, Y = CH_2OH **3b**

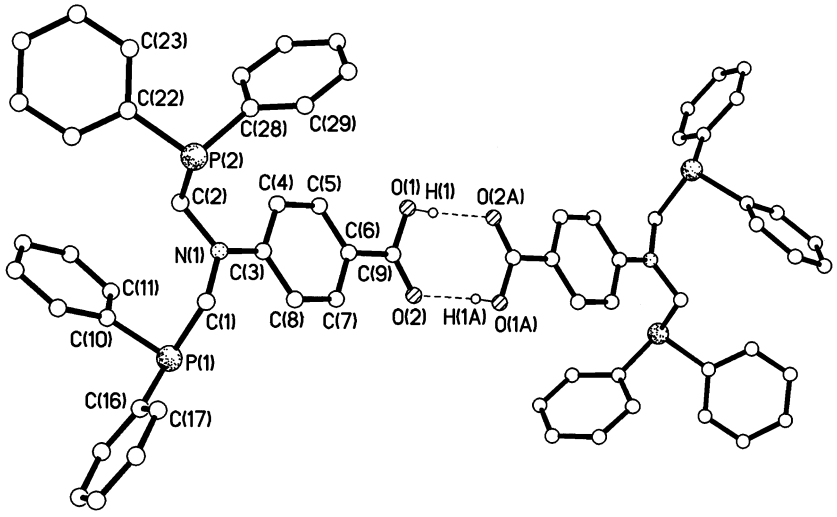


Figure 1. X-Ray structure of compound **1b** showing (i) the molecular structure and (ii) the intermolecular carboxylate head-to-tail H-bonding motif giving rise to dimer pairs.

Ph_2P- groups adopt an *anti* configuration with respect to each other. Strong H-bonding, via the carboxylate groups, is also evident and links molecules into head-to-tail dimer pairs through hydrogen bonding [O(1)···O(2A) 2.670(1) Å, H(1)···O(2A) 1.85(2) Å; O(1)–H(1)···O(2A) 171(2)°].

In conclusion, we have developed a facile procedure for the synthesis of new modified ditertiary phosphines bearing various functional groups. This synthetic route is extremely practical with reactions generally complete within a few hours in refluxing CH_3OH. In addition to the short reaction times this method obviates the preparation of reactive intermediates, uses cheap and commercially available starting materials, requires no purification steps nor any stringent need for performing reactions under a rigorously controlled oxygen free atmosphere. Current efforts are directed towards 'tagging' these molecules onto polymeric (including dendrimeric) supports, exploring their co-ordination behaviour and potential utility in catalysis.

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References

1. Stelzer, O.; Langhans, K. P. In *The Chemistry of Organophosphorus Compounds*; Hartley, F. R., Ed.; John Wiley & Sons: New York, 1990; Vol. 1.
2. (a) Doherty, S.; Robins, E. G.; Nieuwenhuyzen, M.; Knight, J. G.; Champkin, P. A.; Clegg, W. *Organometallics* **2002**, *21*, 1383–1399; (b) Shaw, B. L.; Perera, S. D. *Chem. Commun.* **1998**, 1863–1864.
3. Yamagishi, T.; Ikeda, S.; Yatagai, M.; Yamaguchi, M.; Hida, M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1787–1790.
4. Schmidbaur, H.; Paschalidis, C.; Steigelman, O.; Müller, G. *Chem. Ber.* **1989**, *122*, 1851–1855.
5. Brunner, H.; Dylla, M. E.; Hecht, G. A. M.; Pieronczyk, W. *Z. Naturforsch.* **1982**, *37b*, 404–406.
6. Scherer, J.; Huttner, G.; Büchner, M. *Chem. Ber.* **1996**, *129*, 697–713.
7. Smith, M. B.; Elsegood, M. R. J. *Tetrahedron Lett.* **2002**, *43*, 1299–1301.
8. Durran, S. E.; Smith, M. B.; Slawin, A. M. Z.; Steed, J. W. *J. Chem. Soc., Dalton Trans.* **2000**, 2771–2778.
9. Reetz, M. T.; Lohmer, G.; Schwickardi, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1526–1529.
10. Balch, A. L.; Olmstead, M. M.; Rowley, S. P. *Inorg. Chim. Acta* **1990**, *168*, 255–264.