ChemComm

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *Chem. Commun.*, 2018, **54**, 10443

Received 19th July 2018,
Accepted 21st August 2018

DOI: 10.1039/c8cc05890c

rsc.li/chemcomm

1,1-Diphosphines and divinylphosphines *via* base catalyzed hydrophosphination†

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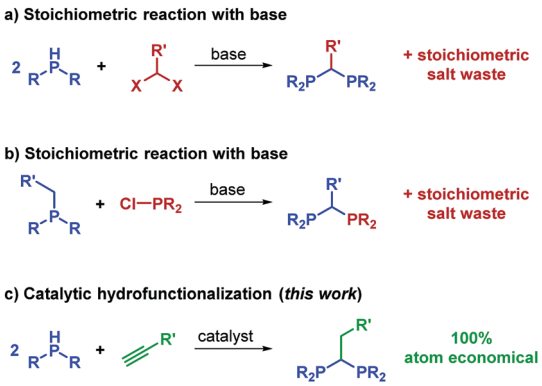
A catalytic hydrophosphination route to 1,1-diphosphines is yet to be reported: these narrow bite angle pro-ligands have been used to great effect as ligands in homogeneous catalysis. We herein demonstrate that terminal alkynes readily undergo double hydrophosphination with $HPPh_2$ and catalytic potassium hexamethyldisilazane (KHMDS) to generate 1,1-diphosphines. A change to H_2PPh leads to the formation of *P,P*-divinyl phosphines.

Bidentate phosphines constitute an immensely important class of compounds used throughout synthetic chemistry, where they are commonly employed as ligands in transition metal catalysis.[1–3] An array of diphosphines have been prepared and the effect of the phosphine bite angle has been studied in catalysis.[4] Narrow bite-angle 1,1-diphosphines, whereby the phosphorus is linked by a single methylene (or methine) group, have been used with great success in catalytic hydrofunctionalization,[5–13] hydrogenation[14–16] and epoxidation,[17–19] to name but three reaction classes. However, unlike many ligand series used in catalysis, reports of a truly diverse homologous series of 1,1-diphosphine compounds are scarce.[20] Commercially available examples of the free ligand are limited to bis(dimethylphosphino)methane (DMPM), bis(dicyclohexylphosphino)methane and bis(diphenylphosphino)-methane (DPM). The range of functionality that can be tolerated is linked to the challenges associated with the synthesis of such pro-ligands: commonly reaction of the deprotonated phosphine with a dihalomethane is necessary (Scheme 1a).[21–24] The α-deprotonation of a methyl-diaryl/alkyl phosphine and subsequent reaction with a chlorophosphine, is also known (Scheme 1b).[25–27] Both methods are synthetically wasteful, but the latter can give access to unsymmetrically substituted 1,1-diphosphines.

The stoichiometric reaction of a base with phosphines and alkynes has been known for many years.[28,29] One of the first examples where a base was used catalytically (25 mol% loading of PhLi) was demonstrated by Märkl and Potthast to prepare phospholes.[30] Bookham and Smithies subsequently performed a comprehensive study regarding hydrophosphination of non-terminal alkynes using 22 mol% KO*t*Bu as the catalyst, but with the addition of NEt_3 as a solvent.[31] The limitations of this reaction lie not only in the fact that only three or four catalytic turnovers per potassium centre were achieved, but also in the lack of selectivity obtained: the phosphinoalkene product was obtained as a mixture of *E* and *Z* isomers and often the reaction was contaminated with tetraphenyldiphosphine, $(Ph_2P)_2$.

We herein report a mild, facile and selective route to a homologous series of 1,1-diphosphines using alkynes and a catalytic amount of KHMDS (Scheme 1c). The most similar reported methodology and range of products of which we are aware has come from Leung. Using ethyl propiolate and but-3-yn-2-one, a chiral template approach was employed by Leung giving a 1 : 2 mixture of the stereoisomeric 1,1-diphosphine ligated Pd complexes.[32] Interestingly, the 1,1-diphosphine Pd-complex was formed using catalytic amounts of NEt_3 but the 1,2-diphosphine Pd-complex was formed in the presence of



Scheme 1 1,1-Diphosphines can be formed from stoichiometric reaction of an organohalide, phosphine and base whereas this work shows that they can also form using catalytic hydrophosphination chemistry.

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† Electronic supplementary information (ESI) available: Synthetic methods, starting material and product analysis data and NMR spectra. CCDC 1849265–1849269 for **1b**, **1f**, **1i**, **1k** and **2a**, respectively. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c8cc05890c

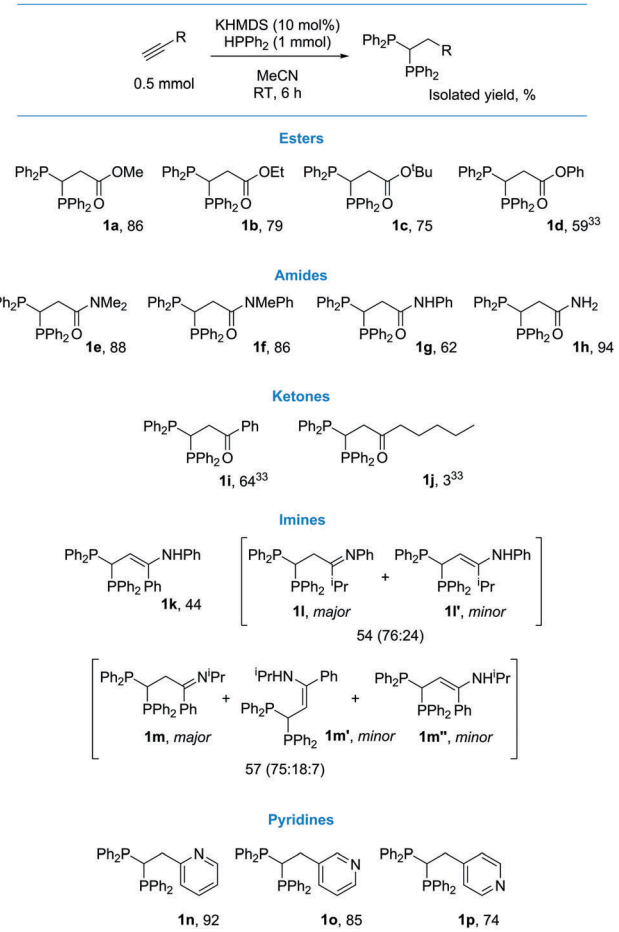
excess NEt_3. HCl (conc.) followed by KCN (aq.) washes were necessary to release the phosphine from the Pd template.

Following a short optimization procedure using ethyl propiolate as our standard substrate, we found that activated alkynes can readily undergo base catalyzed double hydrofunctionalization to yield 1,1-diphosphines at room temperature without the need for any reagents in excess. Weak bases such as K_2CO_3 or NEt_3 do not achieve good selectivity or yield. As an inexpensive and easy to handle base, 10 mol% NaO*t*Bu gives quantitative spectroscopic yield of **1b** in 6 h. Comparable spectroscopic yields of **1b** are also achieved in 6 h using KO*t*Bu, NaHMDS and KHMDS. When the loading of these bases is lowered to 1 mol% it is still possible to achieve very high conversion (>90%, see ESI† for base optimisation). After 16 h at RT in the absence of any base 7% **1b** is obtained along with 49% vinyl phosphine (3 : 1 mixture of *E* and *Z* isomers) and unreacted $HPPh_2$. When we proceeded to investigate reactivity with other alkynes, we found that NaO*t*Bu is not a suitable catalyst. For example, 3-ethynylpyridine only generates **1o** in 17% spectroscopic yield with NaO*t*Bu, a change of alkali metal to KO*t*Bu increases the yield to 38%, but it is only when a change to KHMDS is exercised that a high spectroscopic yield of **1o** is obtained (92%). This is presumably linked to the non-nucleophilic character of KHMDS which leads to cleaner reactivity (multiple side-products are formed from the reaction of NaO*t*Bu and KO*t*Bu). This trend is observed across other classes of substrate: see ESI† for reaction monitoring using NaO*t*Bu, KO*t*Bu and KHMDS with each class of substrate. Hydrophosphination does not proceed in CH_2Cl_2, C_6H_6 or C_6H_5F and thus we investigated substrate scope using 10 mol% KHMDS in MeCN (Scheme 2).

In general, the reaction appears to benefit from carbonyl functionality α to the alkyne and thus other propiolates give high yield of the desired product (**1a** to **1d**[33]). Both tertiary (**1e** and **1f**), secondary (**1g**) and primary (**1h**) propargyl amides and aromatic ketones (**1i**[33]) have been functionalized with good isolated yield. Aliphatic ketones give low yield of product (**1j**[33]). Imines also react well but undergo concomitant tautomerization to give the enamine (**1k** to **1m**/**1m′**/**1m″**). We are pleased to report that ethynylpyridines can be used in the transformation and that the substitution pattern has little bearing on the level of reactivity observed (**1n** to **1p**). Unfortunately, the reaction is not as clean when other aryl acetylenes are employed.[34]

Crystals of **1b**, **1f**, **1i** and **1k** were isolated (see Fig. 1 for **1b** and ESI† for **1f**, **1i** and **1k**). The compounds all have fairly disparate P–C–P bond angles. This is, presumably, linked to sterics of the pendant functional group with the tertiary amide of **1f** providing the greatest steric bulk and therefore forcing the P–C–P bond angle to become more acute (99.41(9)°) than that observed for the ester (**1b**: 103.60(8)°), whereas the phenyl ketone (**1i**) has a wider P–C–P bond angle at 105.75(9)°. These P–C–P bond angles are in-line with that of DPM,[35] which is reported as 106.17°. Enamine **1k** has a wider P–C–P bond angle of 108.53(8)°. It can be surmised that these crystal data indicate that our hydrofunctionalization products are primed for use as ligands in transition metal complexes.

A radical clock study of our standard reaction (0.5 mmol ethyl propiolate, 1 mmol $HPPh_2$, 10 mol% KHMDS, 1 mL MeCN with 1 mmol (chloromethyl)cyclopropane) gives 70% **1b** after 1 h and 98% **1b** after 6 h *i.e.* results that are comparable to those obtained in the absence of a radical clock[34] suggesting a non-radical mediated reaction. During our reaction monitoring studies a small quantity of the *E*-vinyl phosphine moiety is observed by *in situ* NMR spectroscopy after 1 h suggesting that this is the (sterically driven) product of the first hydrophosphination and the



Scheme 2 1,1-Diphosphines formed from the reaction of functionalized acetylenes with $HPPh_2$ in the presence of 10 mol% KHMDS.

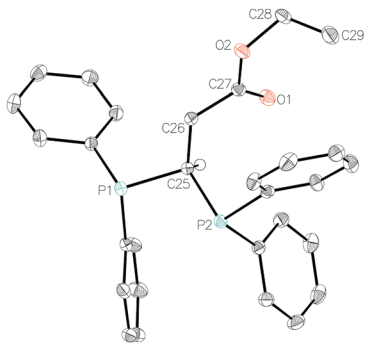
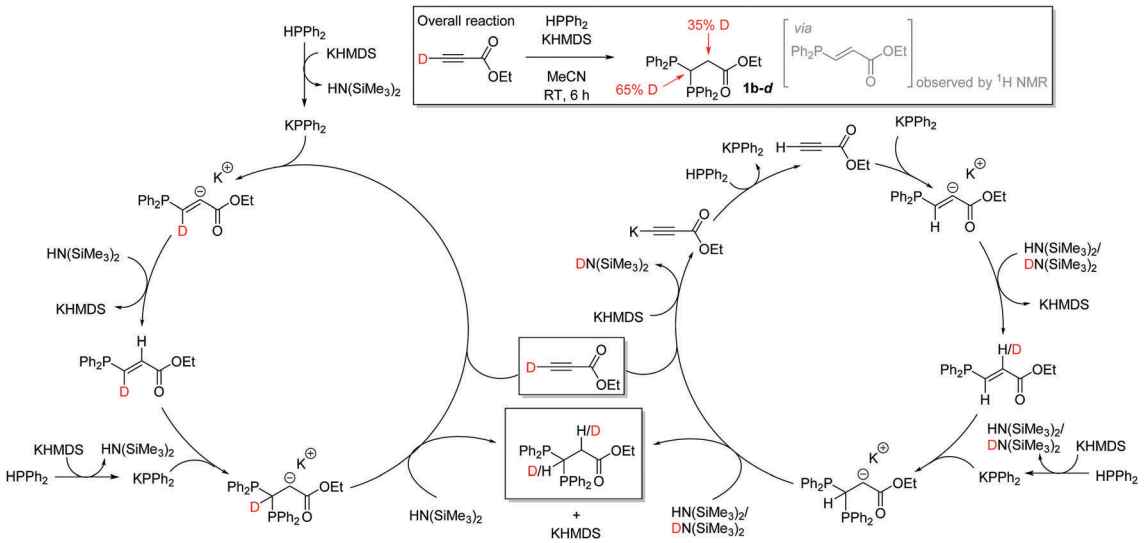


Fig. 1 Molecular structure of **1b**. Ellipsoids are represented at 30%. With the exception of the methine proton, all hydrogen atoms have been omitted for clarity.

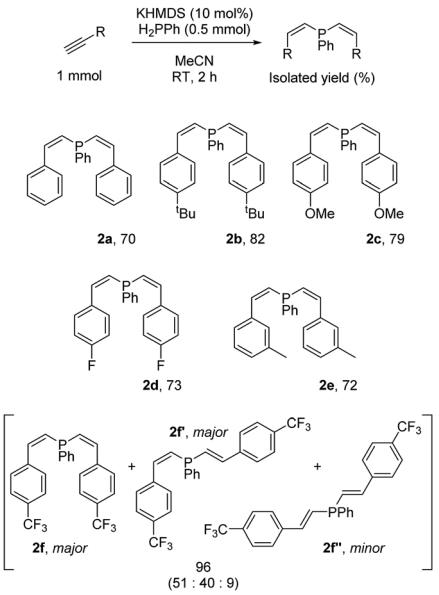


Scheme 3 Results of deuterium labelling study and proposed catalytic cycle, with potential route by which deuteration could occur at the methylene position (right hand cycle).

Michael accepting properties of this phosphinoalkene then facilitate the regioselective second hydrophosphination reaction. To further investigate the role of the base, ethyl propiolate-*d* was used in a catalytic reaction. Deuterium is observed at both the methine and methylene positions of **1b-*d***. Order of addition of reagents/catalyst do not appear to impact on the reaction. $HPPh_2$ and ethyl propiolate-*d* do not undergo H/D exchange in the absence of KHMDS. Given the acidity of the propargylic proton, we believe that competitive deprotonation of this moiety takes place which can lead to deuteration of both methylene and methine carbons (Scheme 3).

By changing the phosphine to a primary phosphine (H_2PPh), we are able to afford divinylphosphines in the *Z*,*Z* configuration, with only one exception (Scheme 4). *P*,*P*-Divinyl phosphines have only previously been reported by Issleib using the potassium salt of phenylphosphine and appeared to give a mixture of isomers,[29] or by Kobayashi who used AIBN but obtained a mixture of isomers (52% *Z*,*Z*, 30% *Z*,*E* and 18% *E*,*E*).[36] More recently Takahashi used cross-coupling, rather than a hydrofunctionalization approach, employing phenyl- and *n*-hexyl-vinylzirconocene reagents (where the *E*-geometry was predefined) and dichlorophenylphosphine to afford the *E*,*E* divinylphosphine product.[37] The transformation we report here complements the Zr-catalyzed method of Waterman, whereby internal alkynes undergo mono-hydrophospination with H_2PPh to yield a mixture of *E*- and *Z*-vinylic secondary phosphine or with a prolonged reaction time, the 1,2-diphosphinoalkane.[38]

In contrast to our chemistry with $HPPh_2$ (*vide supra*), the KHMDS catalyzed transformation with H_2PPh is limited to aryl acetylenes: when propiolates are employed complex mixtures form of what appears to be polymeric material. Phenyl acetylene and 4-*tert*-butylphenylacetylene react well, giving products **2a** and **2b** in high isolated yield. Crystals of **2a** could be isolated and display carbon–carbon double bonds of 1.327(4) Å and 1.334(3) Å for C7–C8 and C15–C16 respectively and a C7–P1–C15 bond angle of 102.4(1)° (Fig. 2).



Scheme 4 Substrate scope of double hydrophosphination of aryl acetylenes using H_2PPh.

Phenyl rings substituted with electronically challenging groups selectively give the targeted products (**2c** and **2d**). When a

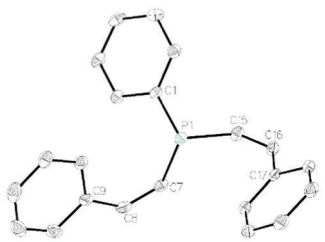


Fig. 2 Molecular structure of **2a**. Ellipsoids are represented at 30%.

highly electron withdrawing 4-trifluoromethyl group is introduced to the aromatic ring a mixture of *E*- and *Z*-products form (**2f**, **2f′** and **2f″**). Mixtures of this type are not observed with the other aryl substrates. All products are obtained in near quantitative spectroscopic yield (>95%) and loss of product occurs due to the sensitivity of these vinyl phosphines.

In summary, we have presented a mild and rapid route to highly functionalized 1,1-diphosphines. NaO*t*Bu, as an inexpensive and easy to handle base, can be used to transform simple propiolates into their 1,1-diphosphine congeners, with a high yield achieved even at 1 mol% loading. However, KHMDS is necessary for more challenging substrates. A change in phosphine reagent from diphenylphosphine to phenylphosphine results in a change in reactivity, allowing the selective formation of *P*,*P*-divinylphosphines. Both sets of products offer intriguing potential modes of reactivity: we envisage using some of our 1,1-diphosphines as bifunctional ligands for heterobimetallic complexes, whilst our divinylphosphines give facile access to monomers for the preparation of phosphorus-containing polymers. Both of these aspects are currently under investigation in our laboratory.

The University of Bath is thanked for a studentship (NTC). The EPSRC UK National Mass Spectrometry Facility at Swansea University is thanked for mass spectrometry analyses. This research was funded through an EPSRC Fellowship EP/P024254/1 (RLW). Crystallization of **1b** was undertaken by Kimberley J. Gallagher.

Conflicts of interest

There are no conflicts to declare.

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