Phosphorus–carbon bond formation catalysed by electrophilic *N*-heterocyclic phosphines

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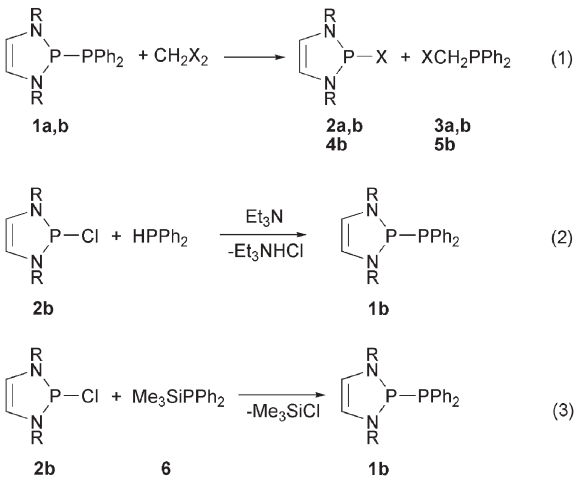
Received (in Cambridge, UK) 13th April 2006, Accepted 18th May 2006
First published as an Advance Article on the web 31st May 2006
DOI: 10.1039/b605278a

A *P*-chloro-diazaphospholene catalyses the phosphorus–carbon bond formation reaction between diphenylsilylphosphine and various alkyl chlorides.

The use of phosphorus compounds in catalysis is clearly dominated by the application of phosphines and phosphine oxides as auxiliary ligands that can support and control the reactivity of a catalytically active metal atom. In addition, there is a steadily increasing number of reports on reactions where phosphines or phosphine oxides are themselves involved as active species.[1] Prominent examples of such "organocatalytic" transformations[2] are Michael additions of activated alkenes or alkynes, or the coupling of activated alkenes with aldehydes (Morita–Baylis–Hillman reaction). A common principle of all these uses of phosphines in catalysis is that their function is closely related to their behaviour as nucleophiles.[1]

Considering that Lewis acids also make important catalysts, phosphorus-based electrophiles such as phosphenium ions, $[R_2P]^+$,[3] might likewise be of interest in catalysis. However, even though the application of these species as powerful Lewis acceptors in stoichiometric reactions is now well documented,[3,4] catalytic applications of phosphorus-based electrophiles remain unexplored. We have recently established that the unique stability of *N*-heterocyclic diazaphospholenium cations induces a significant polarisation of the P–P bond in *P*-phosphinyl-diazaphospholenes and enables stoichiometric bond metathesis reactions in which these derivatives behave as "phosphenium-phosphides" and are capable of transferring a phosphinyl moiety to a substrate.[5] Here, we will demonstrate the use of phosphinyl-diazaphospholenes as catalysts that promote P–C bond formation during the coupling of a silyl phosphine with alkyl halides, and will provide evidence that the recycling of a stable *N*-heterocyclic phosphenium fragment plays an essential role in the reaction mechanism.

It has previously been established that solvolysis of the *P*-phosphinyl-diazaphospholene **1a** in CH_2Cl_2 proceeds *via* bond metathesis to afford the *P*-chloro-diazaphospholene **2a** and the chloromethyl phosphine **3a** (reaction (1), Scheme 1).[5] We have now found that quantitative metathesis is likewise observed when the reaction of **1b**† with a stoichiometric amount of a functional alkyl halide such as CH_2Cl_2 or CH_2I_2, respectively, is carried out in an inert solvent like toluene. The *P*-halogeno-diazaphospholenes **2b** and **4b**, formed as by-products, precipitate from the reaction mixture and are easily removed by filtration, and the pure



Scheme 1 R = t-Bu (**1a–3a**), 2,6-$Me_2C_6H_3$ (**1b–5b**); X = Cl (**2a**,**b**, **3a**,**b**), I (**4b**, **5b**).

α-haloalkyl diphenylphosphines **3b** and **5b** are readily isolated after evaporation of the filtrates.‡

The first syntheses of the diphosphines **1a**,**b** had been accomplished by salt elimination from **2a**,**b** and lithium diphenylphosphide.[5] Further studies revealed now that **1b** is likewise accessible from the coupling of **2b** with diphenylphosphine in the presence of a tertiary amine (reaction (2), Scheme 1), or with trimethylsilyldiphenylphosphine **6** (reaction (3), Scheme 1). Monitoring the progress of the reaction by ^{31}P NMR spectroscopy disclosed that the dechlorosilylation occurred virtually instantaneously and afforded a near quantitative yield of diphosphine **1b** beside minor amounts of side products arising from hydrolytic decomposition of either starting materials or products. In contrast, the dehydrohalogenation required several hours to go to completion and yielded larger amounts of side products.

It becomes immediately evident from inspection of Scheme 1 that the combination of reactions (1) and (2) is equivalent to the *P*-alkylation of diphenylphosphine by coupling with an alkyl halide *via* base-induced elimination of hydrogen chloride. Likewise, the combination of reactions (1) and (3) represents the generation of a tertiary phosphine from the silyl phosphine **6** and an alkyl halide *via* dechlorosilylation. Both types of reactions are widely established in the preparation of phosphines and, in particular, the coupling of silyl phosphines with activated organic chlorides has recently been employed as the key step in the synthesis of tailored phosphine ligands for catalytic applications.[6] Considering that the formation of the diphosphine **1b** from **2b** and **6** as well as its conversion into the tertiary phosphines **3b** and **5b**

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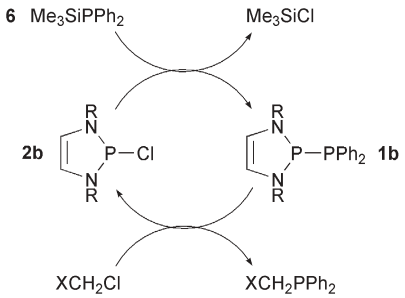

Scheme 2 Diazaphospholene-catalysed cross-coupling of Me_3SiPPh_2 (**6**) with alkyl chlorides XCH_2Cl.

take place under very mild conditions, it is conceivable that a stepwise transformation **6** → **1b** → **3b** may actually proceed faster than direct alkylation of the silyl phosphine **6**. As the *P*-chloro-diazaphospholene **2b** that is required for the formation of **1b** is regenerated in the alkylation step, the whole process can, under these conditions, be formulated as a cyclic sequence (Scheme 2) which would permit the accomplishment of the acceleration of the phosphorus–carbon bond formation in the presence of a catalytic, rather than a stoichiometric, quantity of a diazaphospholene.

In order to verify this hypothesis we studied the diazaphospholene-catalysed alkylation of silyl phosphine **6** with a range of alkyl chlorides. The reactions were conducted by stirring a toluene solution containing **6**, the appropriate alkyl chloride (2 molar equiv.) and a catalytic amount of the *P*-chloro-diazaphospholene **2b** (20 mol% with respect to **6**), at temperatures between 25 °C and 90 °C, for periods between 24 and 170 h (see Table 1). In each case a control reaction was carried out by performing a separate reaction under identical conditions but without catalyst. All reaction mixtures were analysed by ^{31}P NMR and $^{1}H,^{31}P$ HMQC NMR spectroscopy. The products were identified by the evaluation of characteristic correlation signals in the 2D NMR spectra and by comparison of the observed chemical shifts with those of authentic samples.[8] The yields of products and unreacted starting materials were determined by integration of the appropriate NMR signals. In all cases, the yield of product exceeded the amount of **2b** added, thus proving that the latter acts as a catalyst rather than a stoichiometric reagent. No attempts toward isolation of the products were made, but this should readily be feasible by using the same protocol that was applicable for the isolation of **5b**.‡ Preliminary studies indicate that the catalytic reaction is also suitable for the alkylation of other silyl phosphines.

Table 1 Reaction conditions and yields for cross-coupling reactions of Ph_2PSiMe_3 (**6**) with alkyl chlorides RCl

Entry	R	*T*/°C	Reaction time/h	Catalyst/mol%[a]	Yield of Ph_2PR (%)[b]
1	$-CH_2CO_2Et$	25	24	20	>99
	$-CH_2CO_2Et$	25	24	—	>99
2	$-CH_2CH{=}CH_2$	25	120	20	>99
	$-CH_2CH{=}CH_2$	25	120	—	>99
3	$-CH_2Ph$	50	48	20	90
	$-CH_2Ph$	50	48	—	10
4	$-CH_2CN$	25	72	20	80
	$-CH_2CN$	25	72	—	40
5	$-CH_2Cl$	90	24	20	>99
	$-CH_2Cl$	90	24	—	0
6	n-Bu	90	170	20	90
	n-Bu	90	170	—	0

[a] Given values denote the molar ratios of the catalyst (**2b**) relative to the substrate (**6**). [b] As determined by integration of $^{31}P\{^{1}H\}$ NMR spectra.

The spectroscopically determined yields of products in the individual transformations are listed in Table 1 and reveal that the reactions studied may roughly be divided into three different categories. Highly reactive alkyl chlorides such as chloroacetyl acetate and allyl chloride (entries 1 and 2) were found to give quantitative conversion of **6** into the corresponding tertiary phosphines within 24 h at ambient temperature even without catalyst. Addition of a catalytic amount of **1b** had no visible effect in these cases. Moderately reactive alkyl halides such as benzyl chloride and α-chloroacetonitrile (entries 3 and 4) required longer reaction times or increased reaction temperatures. Formation of minor amounts of the corresponding tertiary phosphines was in this case observed even without catalyst but the yields improved substantially in the presence of a catalytic amount of **1b**. Finally, unreactive alkyl halides such as dichloromethane and chlorobutane (entries 5 and 6) were completely unreactive, even at 90 °C, in the absence of catalyst but afforded 90% or higher yields of the alkylation product in the presence of **1b**. The coupling of **6** with CH_2Cl_2 yielded exclusively the monosubstituted α-chloromethyl-phosphine **3b**; phosphination of the second chlorine atom to afford diphenylphosphinomethane (dppm) was not observable, even when an excess of the silyl phosphine was employed.

^{31}P NMR studies of the catalytic reactions confirmed that the diphosphine **1b** is in fact formed under the reaction conditions and is finally converted back into the *P*-chloro-diazaphospholene **2b** when the silyl phosphine **6** is completely consumed. Apart from **1b**, no further phosphorus-containing reaction intermediates were detected. These observations confirm that the diazaphospholene participates actively in the metathesis reaction and brings about an acceleration of the phosphorus–carbon bond formation process. The data are further in accord with the anticipated mechanism outlined in Scheme 2 and suggest that alkylation of **1b** is presumably the rate determining step. Considering that the overall process relies on the recycling of a Lewis acidic phosphenium fragment $[R_2P^+]$ between the diphosphine **1b** and the *P*-chloro-diazaphospholene **2b**, the crucial factor for the operation of the catalytic cycle is obviously the P–X bond polarisation (X = Cl, PPh_2) in both intermediates, which controls the weakening of the P–X bonds and, at the same time, enhances the nucleophilicity of X;[5,7] the interplay of both effects makes the intermediates behave as "phosphenium-phosphide" complexes and allows easy turnover of the anionic fragments X. As the bond polarisation is intimately connected with the unique stability of diazaphospholenium cations[5,7] it appears that the decisive element for the functioning of the catalysis lies indeed in the characteristics of the electrophilic $[R_2P^+]$ fragment in the intermediates **1b** and **2b** rather than their nucleophilicity.

In summary, it has been demonstrated that the *P*-phosphinyl-diazaphospholene **1b** undergoes not only stoichiometric metathesis with alkyl halides but may also act as an organocatalyst that promotes the formation of a phosphorus–carbon bond in the condensation of a silyl phosphine with alkyl chlorides. The use of a diazaphospholene as catalyst allows such reactions to be conducted at lower temperatures than usual and permits the coupling of a silyl phosphine with unactivated alkyl chlorides

which were previously not amenable to this reaction. The reactions studied present the first example of a catalytic cycle that relies on the recycling of a Lewis acidic diazaphospholenium fragment [R_2P^+], the capability of which to polarise adjacent P–X bonds and thus enhance their reactivity is of central importance. Further studies dealing with the application of the reaction scheme to the controlled coupling of multifunctional substrates and the potential use of diazaphospholenes as catalysts in other metathesis reactions are in progress.

Notes and references

† **1b** was prepared by analogy to **1a**[5] from $LiPPh_2$ and **2b** in 73% yield; mp 132 °C; satisfactory elemental analysis; $^{31}P\{^1H\}$ NMR (C_6D_6): δ = 125.3 (d, $^1J_{PP}$ = 255 Hz), −34.1 (d, $^1J_{PP}$ = 255 Hz).

‡ **5b**: CH_2I_2 (0.5 mol, 134 mg) was added to a solution of **1b** (0.5 mmol, 124 mg) in toluene (5 ml) and the mixture stirred for 4 h. The formed yellow precipitate of **4b** was filtered off and the filtrate evaporated to dryness to afford **5b** as white solid. ^1H NMR (C_6D_6): δ = 7.51–7.43 (m, 4 H, *o*-CH), 7.03–7.08 (m, 6 H, *m*/*p*-CH), 2.49 (s, 2 H, CH_2); $^{31}P\{^1H\}$ NMR (C_6D_6): δ = −26.6; satisfactory elemental analysis.

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