Rhodium(I)-catalysed conjugate phosphination of cyclic α,β-unsaturated ketones with silylphosphines as masked phosphinides†

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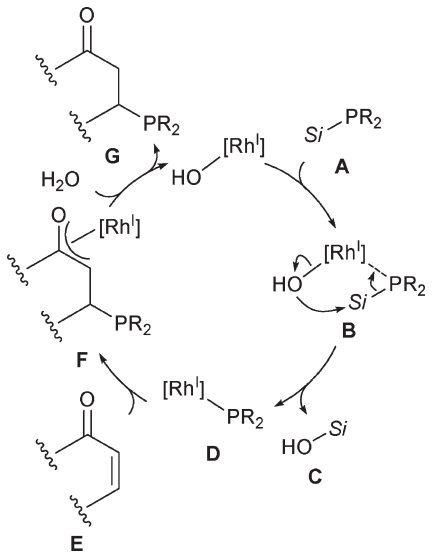
Received (in Cambridge, UK) 24th April 2007, Accepted 22nd May 2007
First published as an Advance Article on the web 11th June 2007
DOI: 10.1039/b706137d

Nucleophile-activation of the phosphorus(III)–silicon linkage in silylphosphines generates a nucleophilic phosphorus(III) equivalent thereby allowing for a rhodium-catalysed conjugate phosphination of β-substituted α,β-unsaturated acceptors.

Transition metal-catalysed addition of element–element bonds, that is linkages between the heavier main group elements, across unsaturated carbon–carbon bond systems is certainly an emerging area in synthetic organic chemistry.[1] Activation of the inter-element linkage[2] is supposed to occur by oxidative addition of the transition metal into the element–element bond[3] or by nucleophile-induced, heterolytic fission of the element–element bond followed by transmetalation to the transition metal.[4] Within the latter mode of action, we recently accomplished the rhodium-catalysed conjugate silyl transfer to cyclic α,β-unsaturated acceptors using a silicon–boron linkage in form of a silylboronic ester as the source of nucleophilic silicon.[4] We currently believe that, in basic aqueous media, a hydroxy-rhodium(I) species nucleophilically attacks at boron thereby facilitating transmetalation of silicon from boron to rhodium with concomitant release of a borate.[5] Based on this putative mechanism, we reasoned that this strategy might be extended to further rhodium-catalysed conjugate addition processes involving nucleophile-induced cleavage of element–element bonds (Scheme 1).

Activation of the phosphorus(III)–silicon linkage in silylphosphines **A**[6] and subsequent conjugate phosphination of α,β-unsaturated carbonyl compounds **E** seemed as a reasonable system to verify this hypothesis (Scheme 1). We therefore proposed that the catalysis will begin with coordination of **A** to the Rh^{I}–OH catalyst[5] (**A** → **B**), in which silicon is prone to intramolecular attack by the nucleophile, Lewis basic oxygen (shown) or hydroxide after deprotonation (not shown) (**B** → **D**). The phosphorus–silicon bond fission at **B** *via* a hypervalent silicon species is directly generating a phosphinide at rhodium(I) along with silane **C**.[7] The unsaturated substrate **E** is then captured by **D** (not shown), and conjugate transfer of phosphorus(III) provides intermediate **F** (**E** → **F**), which liberates the active catalyst upon hydrolysis (**F** → **G**).

While we were examining the above-discussed strategy, Hayashi *et al.* disclosed a rhodium-catalysed phosphination of carbon–carbon triple bonds using **A**.[8] This fine investigation also includes examples of conjugate phosphorus(III) transfer yet limited to



Scheme 1 Working hypothesis: postulated catalytic cycle.

β-unsubstituted acceptors such as ethyl acrylate and acrylonitrile. Apart from this isolated report,[8] examples of conjugate carbon–phosphorus(III) bond formation of *β-substituted* α,β-unsaturated carbonyl compounds are relatively scarce. An uncatalysed 1,4-addition of **A**[9] and a related fluoride-mediated process again using **A**[10] are the sole efforts towards this objective. An excellent article by Enders *et al.*[11] recently summarised the different techniques available for conjugate phosphorus(III) as well as phosphorus(V) transfer, including direct 1,4-addition of lithium phosphinides to *β-substituted* acceptors.[12] In this regard, the 1,4-addition of borane-protected phosphines also attracted interest.[13] Knochel *et al.* described a general potassium *tert*-butoxide-catalysed addition of phosphines to functionalised terminal alkenes.[14]

In this communication, we report a rhodium-catalysed 1,4-addition of *in situ*-generated, diaryl- as well as dialkylsubstituted phosphinides to cyclic α,β-unsaturated ketones. This mild carbon–phosphorus(III) bond forming reaction complements the existing techniques for the preparation of functionalised phosphines.

Silylphosphines **1–3** used in this study were accessed in high yields according to a reported procedure (left, Scheme 2).[15] The related preparation of **4–5** bearing an aryl group at silicon failed though; quantitative formation of the corresponding disilane indicated a lithium–chlorine exchange at silicon. Reversal of the nucleophilicity and electrophilicity of the reaction partners produced these silylphosphines in good yields as well (right, Scheme 2).

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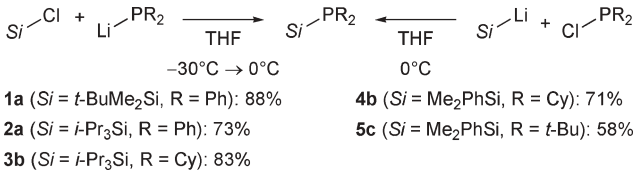
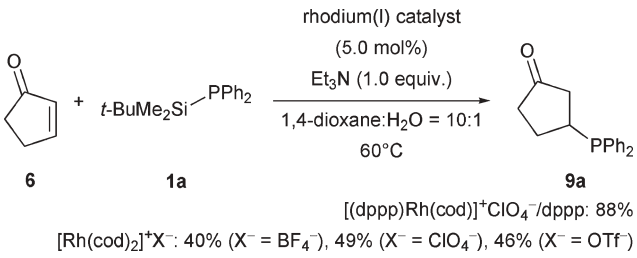
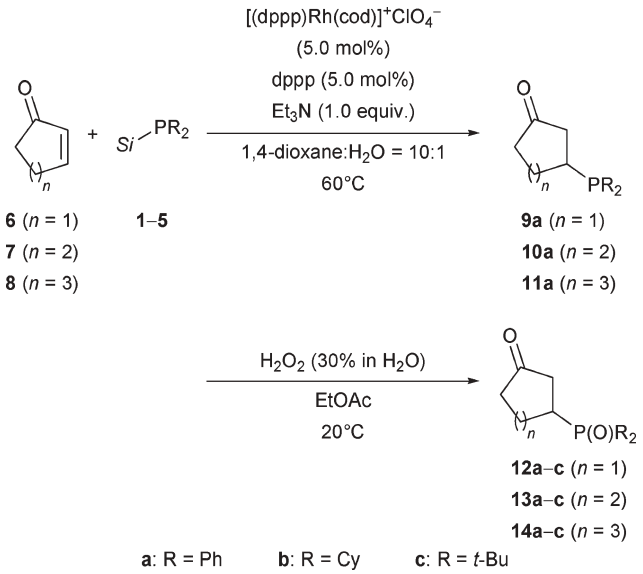
† Electronic supplementary information (ESI) available: Characterisation data as well as ^{1}H, ^{13}C and ^{31}P NMR spectra of all new compounds. See DOI: 10.1039/b706137d



Scheme 2 Preparation of silylphosphines used in this survey.



Scheme 3 Identification of both the rhodium(I) catalyst and the essential base for the phosphinyl transfer.



Scheme 4 Synthesis of β-phosphinyl and β-phosphinoyl cyclic ketones (see Table 1 for details).

In the light of the mechanistic analogy of rhodium-catalysed conjugate silyl and phosphinyl transfer,[4] we chose to start with cationic rhodium(I) complex [(dppp)Rh(cod)]ClO_4/dppp (5.0 mol%).[16] We had previously observed that the presence of strongly coordinating counterions hamper product formation. In fact, weakly or non-coordinating anions (X^- = BF_4^-, ClO_4^- as well as OTf^-) were critical for success. This is in agreement with the above-mentioned report by Hayashi *et al.*,[8] in which chloride-bridged $[Rh(cod)Cl]_2$ required stoichiometric addition of AgOTf in order to generate a catalytically active cationic rhodium(I) catalyst. We were then pleased to find that our catalyst promoted the conjugate phosphination of **6** using conventional silylphosphine **1a** under reaction conditions identical to those of the silyl transfer[4] (**6** → **9a**, Scheme 3).

In a series of control experiments, we were able to show that both a cationic rhodium(I) catalyst and a base are essential for achieving conversion. These findings corroborate that this transformation is not simply base-catalysed but might require the base to form a nucleophile, at least in equilibrium, for the assumed transmetalation step (*vide supra*) (**B** → **D**, Scheme 1).[17] Silylphosphines **A** are likely to coordinate to and thereby stabilise the catalyst (**A** → **B**, Scheme 1). The presence of an additional phosphine ligand (dppp) might therefore be superfluous. However, when using phosphine-free $[Rh(cod)_2]BF_4$ (5.0 mol%) instead of [(dppp)Rh(cod)]ClO_4/dppp (5.0 mol%), phosphinyl transfer from **1a** to **6** proceeded at markedly lower reaction rate affording **9a** in poor yield (Scheme 3). Similar results were obtained for other reagent–substrate combinations. We also note here that conversion is not dependent on the counter anion (X^- = BF_4^-, ClO_4^- or OTf^-) present in the reaction mixture (Scheme 3).[5]

After identification of the suitable catalyst, we continued employing further acceptors **7** and **8** and tested phosphinide sources. Isolated yields were invariably high with **1a** (77–91%) performing slightly better than **2a** (65–80%) (Scheme 4, Table 1, entries 1–6). Diarylsubstituted **9a–11a** were not sensitive toward oxidation during purification; subsequent treatment with hydrogen peroxide prior to flash chromatography gave the corresponding phosphine oxides **12a–14a** in the same yields within the experimental error (Scheme 4 and Table 1, entries 1–6). We also targeted the formation of a carbon–phosphorus bond using the novel silylphosphines **3b**, **4b** and **5c**, which would release a dialkyl- rather than a diarylphosphinyl moiety. Under standard conditions, the cyclic β-dicyclohexylphosphinyl ketones were formed in excellent yields yet isolation of these oxygen-sensitive phosphines by flash chromatography proved difficult. We therefore decided to directly oxidise the intermediate trivalent phosphine, which afforded β-dicyclohexylphosphinoyl ketones **12b–14b** (Scheme 4, Table 1, entries 7–12). The corresponding β-di-*tert*-butylphosphinoyl ketones **12c–14c** were produced in moderate yields following the identical reaction sequence (Table 1, entries 13–15). If the phosphines are desired, purification on larger scale by Kugelrohr distillation is also possible.

In summary, silylphosphines served as protected phosphinides in conjugate carbon–phosphorus bond formation catalysed by a cationic rhodium(I) complex. Extension of this methodology to

Table 1 Conjugate phosphinyl transfer form silylphosphines **1–5** to α,β-unsaturated acceptors **6–8** followed by oxidation‡

Entry	*Si*–PR_2	Acceptor	Phosphine	Yield[a] (%)	Phosphine oxide	Yield[a] (%)
1	**1a**	**6** (*n* = 1)	**9a**	91	**12a**	88
2	**1a**	**7** (*n* = 2)	**10a**	77	**13a**	73
3	**1a**	**8** (*n* = 3)	**11a**	91	**14a**	89
4	**2a**	**6** (*n* = 1)	**9a**	80	**12a**	72
5	**2a**	**7** (*n* = 2)	**10a**	65	**13a**	60
6	**2a**	**8** (*n* = 3)	**11a**	79	**14a**	76
7	**3b**	**6** (*n* = 1)	—	—	**12b**	79
8	**3b**	**7** (*n* = 2)	—	—	**13b**	87
9	**3b**	**8** (*n* = 3)	—	—	**14b**	92
10	**4b**	**6** (*n* = 1)	—	—	**12b**	64
11	**4b**	**7** (*n* = 2)	—	—	**13b**	84
12	**4b**	**8** (*n* = 3)	—	—	**14b**	89
13	**5c**	**6** (*n* = 1)	—	—	**12c**	48
14	**5c**	**7** (*n* = 2)	—	—	**13c**	55
15	**5c**	**8** (*n* = 3)	—	—	**14c**	58

[a] Isolated yield of analytically pure product after flash chromatography.

acyclic acceptors as well as elucidation of the mechanism of action, transmetalation (Rh^{I}–PR_2) or oxidative addition (Rh^{III}–PR_2) reaction pathway, are the current focus of our investigations.

The research was supported by the International Research Training Group Münster–Nagoya (GRK 1143) (predoctoral fellowship to V. T. T., 2007–2009) and the Aventis Foundation (Karl Winnacker fellowship to M. O., 2006–2008). Generous donation of chemicals from Wacker AG (Burghausen/Germany) is gratefully acknowledged.

Notes and references

‡ *General procedure for the preparation of silylphosphines* ***4b*** *and* ***5c***: To a large excess (~10 equiv.) of freshly cut lithium wire (previously activated with Me_3SiCl) in THF (30 mL), dimethylphenylsilyl chloride (4.40 g, 25.8 mmol, 1.00 equiv.) was added in one portion at room temperature under argon atmosphere. The reaction mixture was maintained at −13 °C for 18 h (dark red coloration indicated formation of dimethylphenylsilyllithium). The mixture was allowed to warm to 0 °C and stirred for an additional hour under sonication. In order to separate the dimethylphenylsilyllithium solution from unreacted lithium metal, the supernatant was transferred to a dropping funnel connected to a Schlenk flask *via* a double-ended cannula. The Schlenk flask was then charged with the chlorodialkylphosphine (25.8 mmol, 1.00 equiv.) and *n*-hexane (60 mL) before the anionic lithium species was added slowly over a period of 2 h at 0 °C. The addition was accompanied by a color change and precipitation of LiCl. The reaction mixture was allowed to warm to room temperature and maintained at this temperature for an additional 2 h. After evaporation of the solvents, the residue was purified *via* Kugelrohr distillation. The title compounds gave satisfactory characterisation data (ESI†).*General procedure for the rhodium-catalysed 1,4-addition of α,β-unsaturated cyclic ketones*: Under an argon atmosphere, a Schlenk tube equipped with a magnetic stirring bar was charged with the α,β-unsaturated cyclic acceptor **6–8** (1.0 equiv.) dissolved in deoxygenated 1,4-dioxane–H_2O = 10 : 1 (~0.5 M based on substrate). After addition of [(dppp)Rh(cod)]ClO_4 (5.0 mol%) and dppp (5.0 mol%) or $[Rh(cod)_2]X$ (5.0 mol%), Et_3N (1.0 equiv.) and silylphosphine **1–5** (2.5 equiv.) were successively added. The reaction mixture was maintained at 60 °C for 2 days. Depending on the oxygen-sensitivity of the phosphorus(III) intermediate, one of the following procedures was applied: *Method A* (R = Ph): A small portion of silica gel was added after cooling to room temperature and the solvents were evaporated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (cyclohexane–ethyl acetate = 5 : 1) affording the β-phosphinyl ketones **9a–11a**. *Method B* (R = Ph, Cy and *t*-Bu): The reaction mixture was cooled to room temperature and directly oxidised with H_2O_2 (30%, 2.0 equiv.). After additional stirring for 4 h, H_2O and aqueous $FeSO_4$ (0.5 M) were added. The organic layer was separated and the aqueous phase extracted with *tert*-butyl methyl ether (3 ×). The combined organic phases were dried ($MgSO_4$) and the volatiles removed under reduced pressure. Purification by flash column chromatography on silica gel (ethyl acetate) provided the phosphine oxides **12a–14a**, **12b–14b** and **12c–14c**. All compounds gave satisfactory characterisation data (ESI†).

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