

A Simple Building-Block Route to (Phosphanyl-carbene)palladium Complexes via Intermolecular Addition of Functionalised Phosphanes to Isocyanides

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We present a straightforward protocol for making (phosphanyl-carbene)Pd^{II} complexes. These complexes have bidentate ligands containing an acyclic diamino- or aminooxy-carbene and a phosphane. The synthesis gives good yields (typically 70–90 %) for a variety of complexes (22 compounds). Moreover, it does not require the synthesis of imid-

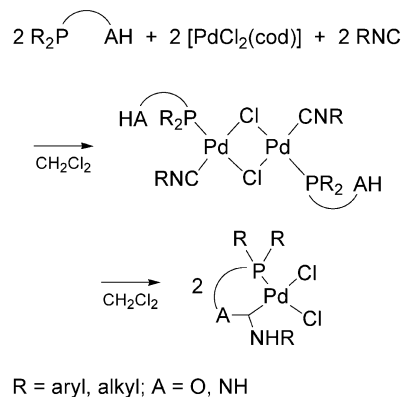
azolium salts nor the a priori generation of free carbenes. Three of the new complexes were tested as catalysts for Sonogashira and Hay coupling reactions, with good yields and selectivities.

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Introduction

The interest in and the importance of carbene-based ligands have grown enormously^[1,2] since Arduengo's seminal discovery in the early 1990s.^[3,4] Carbenes have unique properties as ligands,^[5] with catalytic applications including hydrosilylation,^[6] hydrogenation,^[7,8] and various carbon–element coupling reactions.^[9] Bidentate carbene ligands with a second, other functionality are especially interesting as they combine the strongly coordinating carbene donor with another (more labile) potentially co-ordinating group. The problem is that practical applications of such ligands require simple and straightforward synthesis protocols.^[10] The addition of nucleophiles to coordinated isocyanides, for example, is a facile route to heteroatom-substituted carbenes.^[11–17] It typically involves *intramolecular* addition of a protic polar function onto a carbon–heteroatom moiety, C≡X. Normally, this moiety must be synthesised a priori. Here, we report an alternative protocol that follows *intermolecular* addition of readily available bidentate P–O (or P–N) ligands to simple isocyanides. This intermolecular route enables a building-block synthesis approach, accessing a variety of heteroatom-carbene-Pd complexes. (Scheme 1). We demonstrate this facile synthesis with six-

teen different diamino-carbene-phosphane and aminooxy-carbene-phosphane Pd complexes. Three of these were found to be good precatalysts for Sonogashira and Hay cross-coupling reactions.



Scheme 1. Modular synthetic route towards palladium(II) complexes of diamino- and aminooxycarbene-phosphane ligands.

This novel class of modular, tethered open-chain carbenes is based on the well known idea that isocyanide coordination to a metal center activates the isocyanide carbon, that can then react with a polar function from another molecule.^[10,18,19] By using a bidentate phosphane-amine or a phosphane-alcohol as the nucleophile, we create a new bidentate phosphane-carbene ligand in the first coordination sphere via intermolecular attack of the polar function on the isocyanide.

Using the modified phosphanes 1–6, the phosphorus atom coordinates to the metal, whilst the amine or alcohol reacts with the isocyanide, forming a carbene. In this way one obtains directly and cleanly a bidentate phosphane-

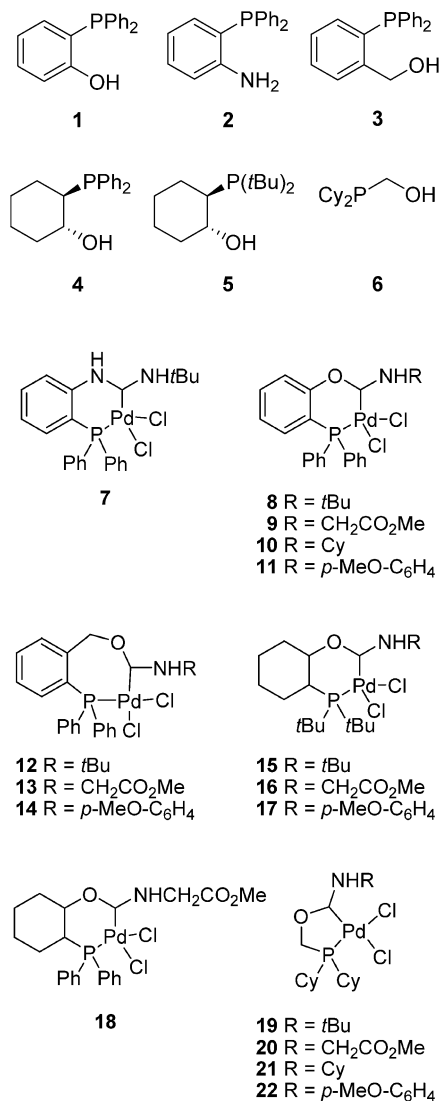
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carbene ligand coordinated to the metal center. Thus, reacting compounds **1–6** with four commercially available isocyanides RNC (R = *t*Bu, Cy, 4-MeOC₆H₄, MeO₂CCH₂) in the presence of [PdCl₂(cod)] provides the new compounds **7–22** in good yields.



In a typical reaction, the functional phosphane dissolved in anhydrous dichloromethane was added to an equimolar amount of [PdCl₂(cod)] dissolved in the same solvent. The mixture was stirred for ca. 1 h at 20 °C. Subsequently, one equivalent of the isocyanide dissolved in dichloromethane was added and the reaction mixture was stirred overnight. The solvent was then removed and the product was washed repeatedly with pentane or diethyl ether. Drying in vacuo yielded the carbene-heteroatom-Pd complexes, which were usually obtained in pure form; in some cases recrystallization from dichloromethane/alkanes was necessary.

Crystals of the (phosphanyl-carbene)PdCl₂ compound **9** were grown from dichloromethane/pentane. The complex crystallizes in the space group *P*2₁/*c* (see structure in Figure 1). Interestingly, the bond length Pd(1)–Cl(2) (Cl *trans* to the carbene) is 2.3513(11) Å, which is significantly

shorter than Pd(1)–Cl(1) (Cl *trans* to P) with 2.3857(10) Å. In view of the relative *trans* influences of the phosphane compared to the carbene, the opposite would be expected. Possibly, the non-ideal angles due to the chelate conformation are responsible for this unusual result.

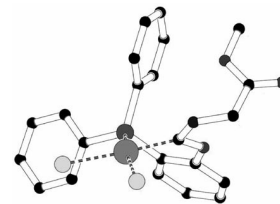


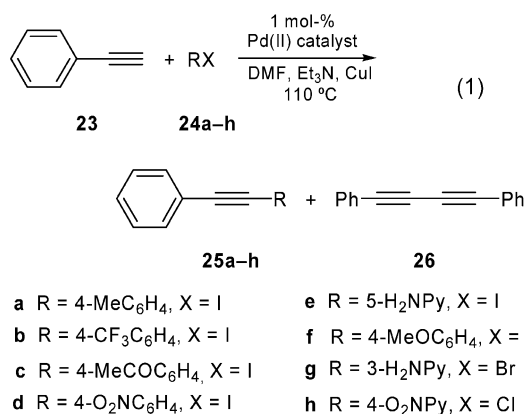
Figure 1. Displacement ellipsoid plot of **9**, drawn at 30% probability level. Pertinent bond lengths [Å] and angles [°]: Pd(1)–Cl(1) 2.3857(10); Pd(1)–Cl(2) 2.3513(11); Pd(1)–P(1) 2.2193(10); Pd(1)–C(4) 1.968(2); Cl(1)–Pd(1)–Cl(2) 91.71(3); Cl(1)–Pd(1)–C(4) 88.16(6); Cl(2)–Pd(1)–P(1) 95.41(3); P(1)–Pd(1)–C(4) 85.17(7).

We tested these new (phosphanyl-carbene)PdCl₂ complexes as precatalysts in the Sonogashira and Hay coupling of various aryl and pyridyl halides. Pyridyl iodides, bromides and chlorides were smoothly coupled with phenylacetylene in the presence of 1 mol-% of Pd-carbene catalyst

Table 1. Pd-carbene-catalyzed Sonogashira and Hay coupling.^[a]

Substrate	Cat.	Conv. (%) ^[b]	Selectivity (%) ^[b]	
			25 (%) ^[b]	26 (%) ^[b]
	None	0	0	0
	11	62	15	47
	15	59	13	46
	21	45	19	26
	11	67	39	28
	15	62	35	27
	21	51	32	19
	11	41	5	36
	15	76	34	42
	21	89	0	89
	11	89	2	87
	21	35	1	34
	11	55	0	55
	21	42	0	42
	15	2	0	2
	21	27	0	27

[a] Reaction conditions: 0.25 mmol aryl or pyridyl halide substrate, 0.38 mmol phenyl acetylene, 0.4 mmol Et₃N, 0.5 mmol CuI and 1 mol-% catalyst relative to **24** in 2.5 mL of DMF at 110 °C for 24 h. [b] Based on GC analysis, corrected for the presence of internal standard.



11, **15** or **21** [Equation (1)]. High selectivity for the Hay product **26** was found for the three catalysts, specifically in the cases of catalysts **15** and **21** with 4-iodoacetophenone, 3-amino-6-iodopyridine and 2-chloro-4-nitropyridine (Table 1).

To discard any possibility of a stoichiometric Stephens–Castro^[20] reaction with copper that would lead to **26**, we ran control experiments without catalyst, both in the presence and absence of halide substrate. No conversion was observed in either case. A selection of bases and additives was also evaluated. For aryl iodides as substrates, the best Hay coupling results were obtained using Et₃N with CuI. Using TBAF with KF, lower conversions were obtained for the bromo and chloro pyridines. In these cases, the selectivity to the Hay product **26** decreased and the Sonogashira product **25** appeared. The Hay product **25** was generally formed with selectivities between 20% and 89% (Table 1) and with TOFs of 60–200 h^{−1}, depending on the catalyst and substrate. Unfortunately, catalytic methoxycarbonylation of ethylene using **7**, **8**, **11**, **12**, **14**, **15** or **21**, failed.

Conclusion

In summary, we have introduced a simple and straightforward route towards Pd^{II} complexes with bidentate ligands containing an acyclic diamino- or aminooxy-carbene and a phosphane. This route allows efficient synthesis of a series of potential catalysts. It does not require the synthesis of imidazolium salts nor the a priori generation of sensitive free carbenes. An intrinsic limitation of this route is that one of substituents on the nitrogen is restricted to be hydrogen. We believe that this modular synthesis of carbene complexes will find many applications in homogeneous catalysis.

Experimental Section

General Procedure for Synthesizing Complexes 7–22: A solution of the relevant phosphane ligand (0.25 mmol) in anhydrous CH₂Cl₂ (5 mL) was added dropwise to a solution of the palladium complex (0.25 mmol) in 5 mL of anhydrous CH₂Cl₂ under nitrogen. The solution was then stirred for 1 h, during which period the colour changed to intense yellow or orange and in some cases a precipitate

may form. Next, a solution of the respective isocyanide (0.25 mmol) in anhydrous CH₂Cl₂ (5 mL) was added dropwise. The colour of the reaction mixture may change to yellow or become colourless. In some cases, the intermediate precipitate redissolves, and a precipitate may form again. In other cases, the product precipitates directly from the homogeneous solution. After stirring overnight, the solvent is removed under vacuum (in case of a precipitate, this may also be filtered off and washed with CH₂Cl₂ and diethyl ether and dried in vacuo). The residue is then suspended in pentane or diethyl ether, washed three times, and dried in vacuo.

Example: Compound **9** (beige solid) yield 72%. ¹H NMR (CD₂Cl₂): δ = 10.68 (s, 1 H), 8.00–6.60 (m, 14 H), 4.07 (s, 2 H), 3.63 (s, 3 H) ppm. ³¹P{¹H} NMR (CD₂Cl₂): δ = 21.5 ppm. FAB-MS: *m/z* = 540 [M⁺ – CH₃], 517 [M⁺ – Cl – 2 H], 482 [M⁺ – 2 Cl – 2 H]. C₂₂H₂₀Cl₂NO₃PPd (554.7): calcd. C 47.63, H 3.63, N 2.52; found C 46.25, H 3.45, N 2.38. Data of all other new compounds have been compiled in the Supporting Information.

Procedure for Sonogashira and Hay Cross-coupling: The reactions were performed in sets of 16 reactions using a Chemspeed Smartstart 16-reactor block, modified in-house for efficient reflux and stirring. GC analysis was performed on an Interscience GC-8000 gas chromatograph with a 100% dimethylpolysiloxane capillary column (DB-1, 30 m × 0.325 mm). GC conditions: isotherm at 105 °C (2 min); ramp at 30 °C min^{−1} to 280 °C; isotherm at 280 °C (5 min). Pentadecane was used as internal standard. All other chemicals were purchased from commercial sources (> 98% pure).

Example: 1-(4-Methoxyphenyl)-2-phenylacetylene (**25f**), catalyst **7**. A Schlenk-type glass vessel equipped with a septum and a magnetic stirrer was charged with phenylacetylene (**23**) (0.38 mmol, 0.042 mL), 4-bromoanisole (**24f**) (0.25 mmol, 0.031 mL), Et₃N (1.6 equiv., 0.4 mmol, 0.056 mL), CuI (2 equiv., 0.5 mmol, 95 mg) and catalyst **7** (1 mol-%, 0.0025 mmol, 1.33 mg) in 2.5 mL of DMF. The reaction mixture was stirred at 110 °C for 24 h under slight N₂ overpressure. Reaction progress was monitored by GC (pentadecane internal standard). Samples for GC were added in equivalent amount of water, extracted with hexane and filtered through an alumina plug prior to injections.

X-ray Crystallographic Study of 9: CCDC-671362 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see also the footnote on the first page of this article): Product yields and analytical data of new compounds and details of the catalytic Sonogashira reactions.

Acknowledgments

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