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Palladacyclic and platinacyclic catalysts for the allylation of aldehydes

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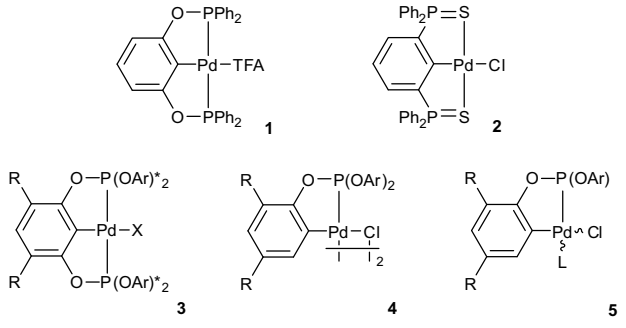
ABSTRACT

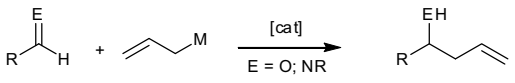
A range of palladacyclic and platinacyclic catalysts have been tested for activity in the allylation of aldehydes with allyl tributyltin. The bulky, π-acidic palladacycle [{Pd(μ-Cl){κ^2-*P*,*C*-P(OC$_6$H$_2$-2,4-^{t}Bu$_2$)-(OC$_6$H$_3$-2,4-^{t}Bu$_2$)}}$_2$] shows particularly good activity at room temperature with a variety of unsaturated substrates.

Catalytic allyl palladium chemistry is a vast field dominated by the reactions of nucleophiles with allyl complexes, by contrast the reactions with electrophilic substrates such as aldehydes and imines (Scheme 1) are less well explored.[1]

Whilst tin reagents are toxic, their ease of handling and the fact that they typically require only mild reaction conditions make them particularly useful allylating reagents for such reactions.[2] Recent work by the groups of Szabó and le Floch showed that palladium 'ECE'-pincer complexes, such as **1** and **2** are very useful catalysts for the reactions of allyl tin reagents with aldehydes and imines.[3,4]



The chiral phosphite-based pincer complexes **3** have been found to show both good activity and modest to good enantioselectivity in the allylation of aldehydes and imines.[5] Unfortunately, the syntheses of bis(phosphite) pincer complexes can be hampered by the challenging C–H activation of the parent ligand or alternatively the need to introduce a halogen onto the resorcinol backbone of the ligand to facilitate complex formation via C–X oxidative addition. By contrast, the synthesis of closely related orthopalladated triarylphosphite complexes of the type **4** and their adducts **5** is facile and these species have been shown to be active catalysts for the conjugate addition reactions of both arylboronic acids and arylsiloxanes.[6] We were therefore interested to see if these systems would act as good catalysts for the allylation of aldehydes with allyl tin reagents; this indeed turns out to be the case and the preliminary findings of this study are presented below.



Scheme 1. Nucleophilic allylation of aldehydes and imines.

In the first instance we investigated the allylation of benzaldehyde with allyltributyl tin using a range of palladacyclic catalysts and the results from this study are summarised in Table 1. As can be seen, the bulky triarylphosphite complex **4a** gave good activity at room temperature, giving a 93% spectroscopic yield of phenylbut-3-ene-1-ol within 24 h at 5 mol % Pd. When the reaction was repeated under air a significant loss in activity resulted (entry 2). In general the reaction times were not optimised, but when the reaction was run for a shorter period (8 h) then the alcohol was produced in only 63% spectroscopic yield (entry 3). When the reaction was performed at 50 °C then a 75% product yield was obtained after 4 h (entry 4). Dichloromethane proved to be the solvent of choice for the reactions; all other solvents tried (entries 5–9) led to reduced or no reaction.

Reducing the size of the orthometallated ring (entry 11) is deleterious to catalyst performance. By contrast, the more electron-rich phosphinite complex **5** showed only a slight reduction in performance (entry 12). The nitrogen based-palladacycles **6** and **7** performed poorly, but surprisingly showed some activity, in contrast with the arylation of enones by arylboronic acids where no activity is observed with these or related complexes.[6a,7] The platinacyclic analogue of **4a**, complex **8**, showed reduced activity compared with the palladium complex as has been noted previously for Lewis acid catalysis using either metallacycles or 'PCP'-pincer complexes.[6a,8]

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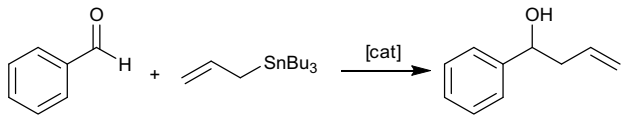
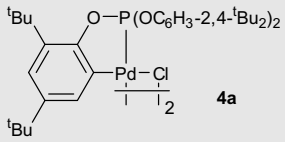
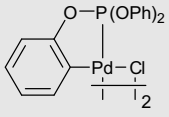
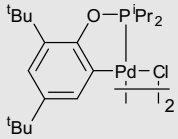
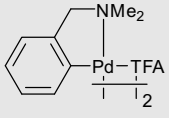
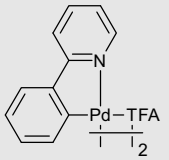
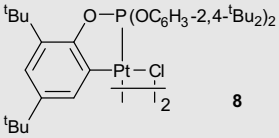
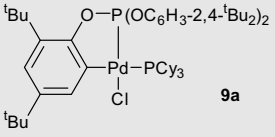
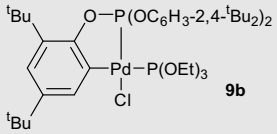
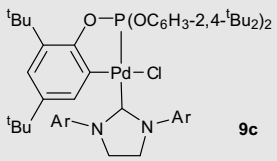
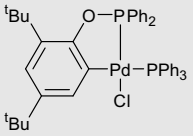
Table 1
Catalyst screening[a]



Entry	Catalyst	Solvent	Yield[b] (%)
1	 **4a**	Dichloromethane	93
2			58[c]
3			63[d]
4			75[e]
5		Toluene	0
6		1,4-Dioxane	33
7		Diethyl ether	48
8		Acetonitrile	42
9		Tetrahydrofuran	35
10		Dichloromethane	28[f]
11	 **4b**		60
12	 **5**		85
13	 **6**		39
14	 **7**		36
15	 **8**		45
16	 **9a**		25
17	 **9b**		17
18	 **9c**		32

Ar = C_6H_3-2,6-^{i}Pr$_2$

Table 1 (*continued*)

Entry	Catalyst	Solvent	Yield[b] (%)
19	 **10**		41
20	[$PdCl_2${P(OC_6H_3-2,4-^{t}Bu$_2$)$_3$}$_2$], **11**		14

[a] Conditions: PhCHO (0.5 mmol), $C_3H_5SnBu_3$ (0.64 mmol), solvent (2 ml), rt 24 h.
[b] Spectroscopic yield determined by ^{1}H NMR ($CDCl_3$, 300 MHz) spectroscopy (1,3,5-trimethoxybenzene internal standard).
[c] Under air
[d] 8 h reaction time.
[e] 50 °C (sealed tube), 4 h.
[f] 4 h

The phosphine, phosphite and carbene adducts **9a–c** and **10** showed poor to modest activity (entries 16–19), depending on the nature of the co-ligand; in all cases they performed less well than the dimeric complex **4a**. The importance of the orthopalladation of the phosphite ligand is demonstrated by the low activity observed with the non-orthometallated complex **11** (entry 20).

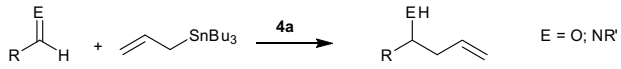
Having established that complex **4a** shows the best activity, this catalyst was then used in the reaction of allyltributyltin with a range of aldehydes and the results are summarised in Table 2.[9] Good to excellent activity was observed with all the aryl aldehydes used. The introduction of methoxy groups on the aromatic ring led to a lowering of yields (entries 5 and 6) as did the introduction of *ortho*-substituents. The catalyst is tolerant of aryl halide, hydroxyl[10] and ferrocenyl functions. The tolerance to bromide is particularly noteworthy when it is considered that the palladacyclic catalyst **4a** is an excellent pre-catalyst for Suzuki, Stille and Heck reactions of aryl bromides at elevated reaction temperatures.[11] A control experiment performed with the electronically activated substrate 4-chlorobenzaldehyde (entry 3) showed no reaction in the absence of catalyst.[12]

In addition to the aryl aldehydes tested, alkyl aldehydes can be used as substrates (entries 15 and 16) albeit with lower yields obtained. The reaction with *N*-benzylidene tosylamine was attempted, but the result obtained was disappointing (entry 17).

With regards to the mechanism, when pincer complexes are used as catalysts Szabó postulates the formation of an intermediate η^1-allyl complex which subsequently reacts with the electrophilic partner,[3] whilst Le Floch favours a Lewis acidic pathway in which a cationic intermediate with a coordinated aldehyde reacts with the allyl tin reagent.[4] By contrast, we find that complex **4a** readily reacts with allyltributyl tin to give the η^3-allyl complex **12** (Scheme 2) and suspect that this is a probable catalytic intermediate.[13] The ^{31}P NMR spectrum of the reaction mixture shows the presence of a new peak at 151.9 ppm, this low field chemical shift is consistent with an orthopalladated triarylphosphite complex.[14] The ^{1}H NMR spectrum of **12** is consistent with an η^3-allyl complex.[15] Subsequent addition of benzaldehyde shows a reduction in the amount of **12** and the concomitant reformation of **4a** (determined by ^{31}P NMR spectroscopy). This is presumably due to the reaction of the putative intermediate **13** with the $ClSnBu_3$ produced during the formation of **12** (Scheme 2).

The reaction sequence outlined in Scheme 2 is consistent with the formation of an η^3-allyl intermediate being the first step in the catalytic cycle, followed by reaction with the aldehyde. It is not possible at this stage to comment on whether this second step proceeds via a five-coordinate transition state with an η^3-allyl

Table 2
Allylation of aldehydes and imines[a]



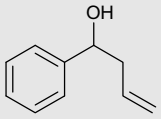
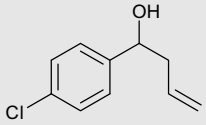
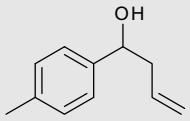
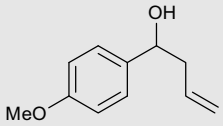
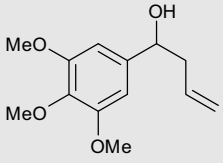
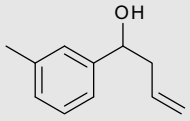
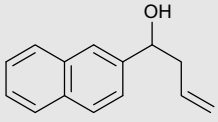
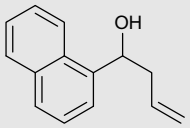
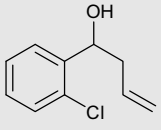
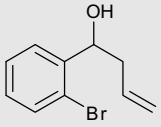
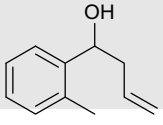
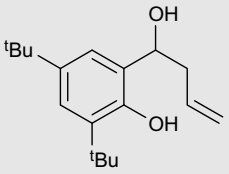
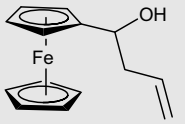
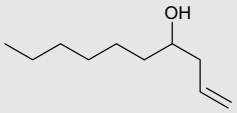
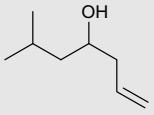
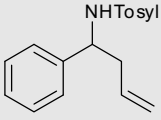
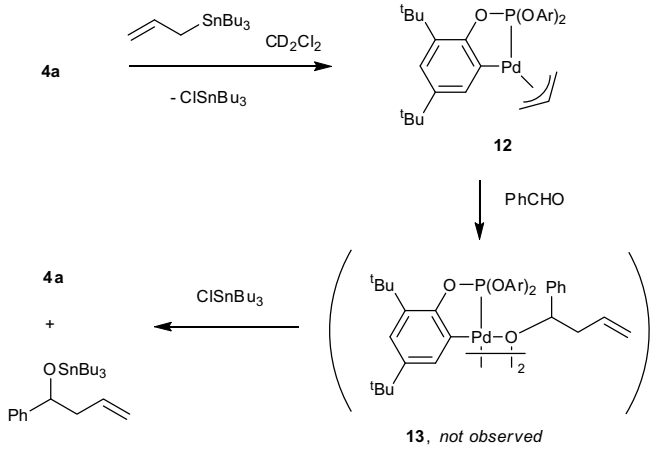
Entry	Product	Yield[b] (%)
1		93
2		95
3		0[c]
4		95
5		73
6		50
7		85
8		88
9		77
10		68
11		71 (63)[d]
12		31

Table 2 (*continued*)

Entry	Product	Yield[b] (%)
13		62 (51)[d]
14		34
15		59
16		33
17		27

[a] Conditions: aldehyde (0.5 mmol), $C_3H_5SnBu_3$ (0.64 mmol), solvent (2 ml), rt 24 h.
[b] Spectroscopic yield determined by ^1H NMR ($CDCl_3$, 300 MHz) spectroscopy (1,3,5-trimethoxybenzene internal standard).
[c] No catalyst.
[d] Isolated yield.



Scheme 2.

ligand, or a four-coordinate species with an η^1-allyl ligand. Further studies are in progress to resolve this issue.

In summary, the simple, commercially available[16] palladacyclic complex **4a** is an active catalyst for the allylation of aldehydes with allyltributyl tin under mild conditions.

Acknowledgements

We thank the EPSRC (Advanced Research Fellowship for RBB, DTA studentship for LTP) for funding, Johnson Matthey for funding

and the loan of precious metal salts and Dr. Chris Barnard (Johnson Matthey) for useful discussions.

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8. Longmire, J. M.; Zhang, X.; Shang, M. *Organometallics* **1998**, *17*, 4374.
9. General method for catalysis: A solution of aldehyde or imine (0.5 mmol), $C_3H_5SnBu_3$ (0.20 ml, 0.64 mmol) and catalyst (5 mol %), in CH_2Cl_2 (2 ml) was stirred at room temperature for 24 h. The reaction mixture was quenched with water (10 ml), the product extracted with CH_2Cl_2 (3×10 ml), the combined organic phase dried ($MgSO_4$) and the solvent removed under reduced pressure. 1,3,5-Trimethoxybenzene (internal standard, 28 mg) was added and the yield was determined by ^{1}H NMR spectroscopy ($CDCl_3$, 300 MHz).
10. NMR data for the product (Table 2, entry 13): ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.28 (s, 9H, ^{t}Bu), 1.42 (s, 9H, ^{t}Bu), 2.52–2.82 (m, 2H, CH_2), 4.84 (ddd, 1H, J = 9.22, 4.46, 2.49, ArC*H*(OH)CH_2), 5.20–5.30 (m, 2H, CH=CH_2), 5.80–5.96 (m, 1H, CH=CH_2), 6.83 (d, 1H, J = 2.49, OH), 7.23 (s, 1H, Ar*H*), 7.24 (s, 1H, Ar*H*), 8.19 (s, 1H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 29.8, 31.7, 34.3, 35.2, 41.8, 76.0, 119.4, 122.0, 123.6, 125.5, 134.5, 137.0, 141.3, 152.6.
11. (a) Albisson, D. A.; Bedford, R. B.; Lawrence, S. E.; Scully, P. N. *Chem. Commun.* **1998**, 2095; (b) Albisson, D. A.; Bedford, R. B.; Scully, P. N. *Tetrahedron Lett.* **1998**, *39*, 9793; (c) Bedford, R. B.; Hazelwood, S. L.; Limmert, M. E.; Albisson, D. A.; Draper, S. M.; Scully, P. N.; Coles, S. J.; Hursthouse, M. B. *Chem. Eur. J.* **2003**, *9*, 3216.
12. Le Floch and co-workers showed low levels of background reaction in the absence of catalyst with *p*-nitrobenzaldehyde as substrate at room temperature, see Ref. 4.
13. Complex **12** can also be produced by the reaction of **4a** with allyl magnesium bromide.
14. Samples of **12** are moisture sensitive as demonstrated by ^{31}P NMR spectroscopy which shows small amounts of two isomers of a hydrolysis product at δ 120.3 and 119.8 ppm, minor and major isomers, respectively. Addition of water to complex **12** leads to rapid formation of this product. The similarity of the chemical shifts compared with **4a** suggests that this may be the hydroxyl bridged analogue.
15. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.70 (dd, J = 2.4 and 1.5 Hz, 1H, H6 orthometallated ring), 7.37 (dd, $^4J_{HH}$ = 2.6 Hz, $^5J_{PH}$ = 1 Hz, 2H, H3 non-metallated ring), 7.35 (dd, $^4J_{HH}$ = 2.6 Hz, $^5J_{PH}$ = 1 Hz, 2H, H3′ non-metallated ring), 7.23 (dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{PH}$ = 1.7 Hz, 2H, H6 non-metallated ring), 7.20 (dd, $^3J_{HH}$ = 8.5 Hz, $^4J_{PH}$ = 2.1 Hz, 2H, H6′ non-metallated ring), 7.08 (partially obscured, 1H, H4 orthometallated ring), 7.06 (dd, $^3J_{HH}$ = 8.7 Hz, $^4J_{HH}$ = 2.7 Hz, 2H, H5 non-metallated ring), 7.02 (dd, $^3J_{HH}$ = 8.5 Hz, $^4J_{HH}$ = 2.5 Hz, 2H, H5′ non-metallated ring), 5.27 (m, 1H, allyl central H), 3.71 (m, 2H allyl *syn* Hs), 3.15 (apparent t, J = 14.4 Hz, 1H, allyl *anti* H), 2.19 (dd, $^3J_{HH}$ = 14.1 Hz, $^2J_{PH}$ = 2.9 Hz, 1H, allyl *anti* H), 1.41, 1.39, 1.31, 1.25, 1.24, 1.20 (s, 9H, ^{t}Bu).
16. Sigma–Aldrich and Johnson Matthey Catalysts.