

The first insoluble polymer-bound palladium complexes of 2-pyridyldiphenylphosphine: highly efficient catalysts for the alkoxy carbonylation of terminal alkynes†

Simon Doherty,* Julian G. Knight* and Michael Betham

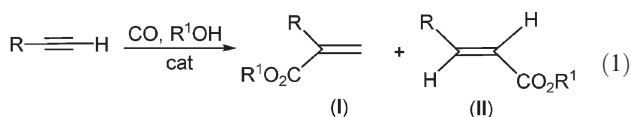
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Palladium complexes of 2-pyridyldiphenylphosphine anchored on polystyrene, polymethylmethacrylate and styrene-methylmethacrylate copolymer form highly active heterogeneous catalysts for the alkoxy carbonylation of terminal alkynes with activities approaching those obtained under homogeneous conditions.

The regioselective palladium catalysed inter- and intramolecular alkoxy carbonylation of terminal alkynes has proven to be a highly versatile process for the synthesis of acyclic and cyclic α,β -unsaturated esters (eqn (1)).¹ Some time ago researchers at Shell discovered that catalysts formed by combining 2-pyridyldiphenylphosphine (2-pyPPh₂), a source of palladium(II) and a sulfonic acid were highly active and selective for the methoxycarbonylation of propyne, giving turn over numbers as high as 40,000 molproduct molcat⁻¹ h⁻¹ with a selectivity for methyl methacrylate (MMA) of 99.95% under mild conditions.²



The use of 2-pyPPh₂ in the palladium catalysed alkoxy carbonylation of alkynes is an exceptional example of a ligand that plays a dual role achieving high selectivity through its ability to function as a bidentate P,N-coordinated ligand while a second P-coordinated N-protonated 2-pyPPh₂ facilitates rapid proton transfer in the rate determining protonolysis step. The critical role of the pyridyl group becomes clearly evident upon replacement of 2-pyPPh₂ by triphenylphosphine, which results in a dramatic decrease in catalyst activity to *ca.* 10 molproduct molcat⁻¹ h⁻¹ as well as a marked reduction in selectivity to 89%.² Given the potential impact of this process for the commercial production of MMA, a large scale (2 × 10⁶ tonnes per annum) industrial intermediate for the production of homopolymers and copolymers,³ as well as for the preparation of fine chemicals,⁴ there is likely to be interest in the immobilisation of 2-pyPPh₂ to develop a continuous process which would combine high catalyst activity and selectivity with facile product separation, in which catalyst leaching is limited.

School of Natural Sciences, Chemistry, Bedson Building, University of Newcastle upon Tyne, Newcastle upon Tyne, NE1 7RU, UK.

E-mail: simon.doherty@ncl.ac.uk; j.g.knight@ncl.ac.uk;

Fax: +44 (0) 191 222 6929;

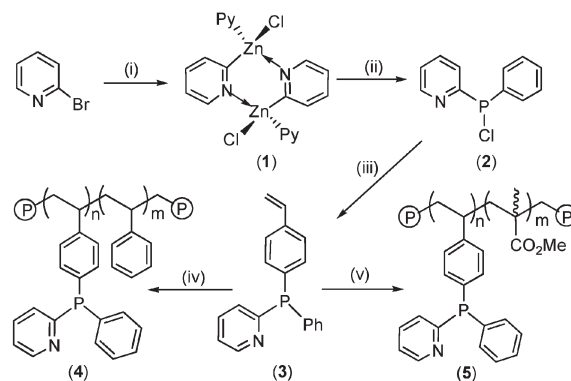
Tel: +44(0) 191 222 6537; +44(0) 191 2227068

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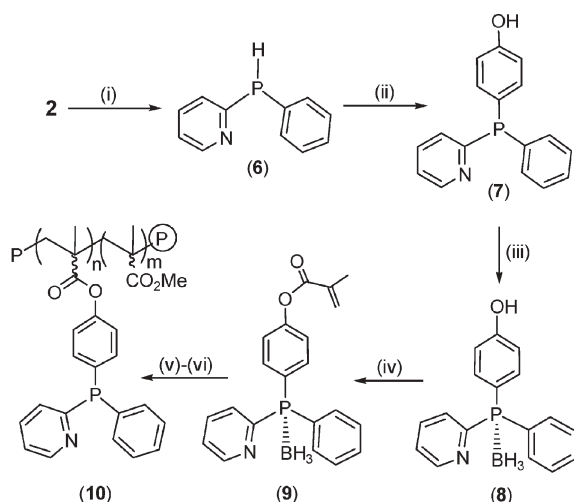
While it is relatively straightforward to immobilise triphenylphosphine⁵ as well as bi-⁶ and terdentate phosphines,⁷ immobilisation of 2-pyPPh₂ to a solid support presents a much greater challenge. Herein, we describe the first example of 2-pyPPh₂ anchored to insoluble polymeric supports and a preliminary investigation of their application to the palladium-catalysed alkoxy carbonylation of terminal alkynes.

The 2-pyridylstyrylphenylphosphine monomer **3** was prepared according to Scheme 1. Lithiation of 2-bromopyridine followed by transmetalation with zinc chloride in pyridine gave the cyclic 2-pyridyl zinc chloride dimer **1**,⁸ which was quenched with dichlorophenylphosphine to afford 2-pyridylphenylchlorophosphine **2**. The polymerisable styryl group was introduced in the final step by reaction of **2** with styryl magnesium chloride. The copolymerisation of **3** with styrene was carried out in benzene using 2,2'-azobis(2-methyl)propionitrile (AIBN) as radical initiator to give polystyrene supported 2-pyridyldiphenylphosphine **4**, as a white solid after precipitation by addition of methanol. Similarly, suspension copolymerisation of **3** with methyl methacrylate gave the corresponding 2-pyridyldiphenylphosphine loaded copolymer **5**. Both polymers have a unimodal molecular weight distribution with polydispersities *M_w/M_n* of 2.1 and 2.0, respectively, and the 2-pyridyldiphenylphosphine loading was determined to be 1.20 and 1.49 mmol g⁻¹, respectively, from elemental analysis.

The 2-pyridyl(*p*-methacryloyloxyphenyl)phenylphosphine monomer **9** was also targeted for the preparation of a 2-pyPPh₂ anchored methacrylate homopolymer and details of the synthesis are outlined in Scheme 2. Initial attempts to reduce **2** with LiAlH₄, NaH and DIBAL all proved unsuccessful either resulting in partial



Scheme 1 Reagents and conditions: (i) BuLi, ZnCl₂, py; (ii) PPhCl₂, THF-py; (iii) styrylMgCl, THF 70 °C; (iv) styrene, AIBN, C₆H₆ (v) MMA, AIBN, C₆H₆.



Scheme 2 Reagents and conditions: (i) Mg, H₂O; (ii) 4-IC₆H₄OH, DMA, 10 mol% Pd(OAc)₂, 70 °C, 12 h; (iii) BH₃-SMe₂, THF, 12 h; (iv) methacryloyl chloride, NEt₃, CH₂Cl₂ -78–0 °C (v) C₆H₆, AIBN, MMA, 60 °C, 12 h (vi) CH₂Cl₂, DABCO, RT 12 h.

reduction or formation of phosphine oxide. Fortunately, the desired secondary phosphine **6** was successfully prepared by careful hydrolysis of the corresponding magnesium phosphide which was readily generated *in situ* from 2-pyridylphenylchlorophosphine and magnesium. A palladium-catalysed cross coupling between 4-iodophenol and **6** was used to introduce the 4-hydroxyphenyl substituent in **7**, which was protected as its borane adduct and reacted with methacryloyl chloride to afford monomer **9**, as a white crystalline air-stable solid. Methacrylate based homopolymer **10** was prepared by copolymerisation of **9** with methyl methacrylate in benzene using AIBN as radical initiator, isolated as an off-white powder by repeated precipitation with methanol and subsequently deprotected with DABCO in dichloromethane. The 2-pyridyl-diphenylphosphine loading in **10** was determined to be 1.42 mmol g⁻¹ from elemental analysis and the polydispersity of 3.8 was measured by gel permeation chromatography.

Catalysts formed by combining polymers **4**, **5** and **10** with palladium acetate were first tested in the methoxycarbonylation of phenylacetylene, the results of which are listed in Table 1. Since the effect on catalyst performance of the amount of acid and ligand has been well documented⁹ investigations were carried out to establish the optimal reaction conditions. The best performance in terms of activity and selectivity was most consistently obtained with L : Pd and acid : Pd mole ratios of 10 and 30, respectively, in agreement with the previous studies of Drent.² Initial studies demonstrated that introduction of a 4-vinyl substituent into 2-pyPPh₂ did not effect catalyst performance since catalysts formed from 2-pyPPh₂ and **3** were both highly active and selective for production of the branched acrylic ester, methyl 2-phenylpropenoate, **1** (entries 1 & 2). The performance of supported catalysts generated from **4**, **5** and **10** and palladium acetate were next investigated and each was found to be highly efficient, giving activities and selectivities approaching those of their homogeneous counterpart (entries 3–5). For each of the polymers, analysis of the reaction mixture after filtration revealed that the palladium content was too low to be detected

Table 1 Methoxycarbonylation of phenylacetylene and propyne^a

Entry	Ligand/support	Substrate ^b	Activity ^c mol product mol cat ⁻¹ h ⁻¹	Selectivity ^d
1	2-pyPPh ₂	PhC≡CH	306	97.4
2	3	PhC≡CH	300	97.1
3	4	PhC≡CH	273	97.5
4	5	PhC≡CH	225	97.3
5	10	PhC≡CH	260	98.0
6	11	PhC≡CH	20	>99.5
7	PPh ₃	PhC≡CH	11.7	81.8
8	12	PhC≡CH	2.0	80.3
9	13	PhC≡CH	4.3	>99.5
11	2-pyPPh ₂	MeC≡CH	1171	97.8
12	3	MeC≡CH	1098	97.7
13	4	MeC≡CH	284	97.9
14	5	MeC≡CH	608	98.0
15	10	MeC≡CH	1022	97.8
16	11	MeC≡CH	55	>99.5
17	13	MeC≡CH	17	>99.5

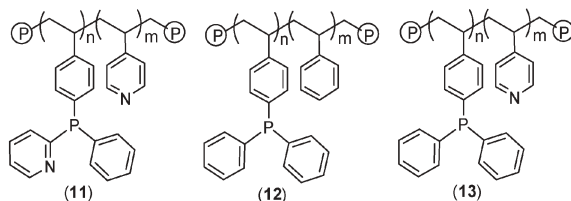
^a Conditions: batch, intake: 30 ml methanol, 40 bar CO, 0.1 mmol ligand, 0.01 mmol Pd(OAc)₂, 0.3 mmol CH₃SO₃H, 50 °C. ^b 10 mmol phenylacetylene or 2.0 bar propyne. ^c Calculated by GC analysis, average of three runs. ^d Determined by GC analysis and ¹H NMR.

by ICP-OES, confirming that leaching was negligible. In addition, the filtered solutions showed no activity indicating that any palladium in solution was either very low in concentration or was in an inactive form.

The high activity and selectivity associated with alkoxycarbonylation of alkynes has been attributed to an active species containing two molecules of 2-pyPPh₂, one of which functions as a bidentate P,N-ligand and is involved in the selectivity determining step while the other coordinates in a monodentate manner and facilitates proton transfer by acting as a cocatalyst in the protonolysis step of the catalytic cycle.^{2,10} In this regard, the performance of these polymer supported catalysts was rather surprising and suggests that copolymers **4**, **5** and **10** have sufficient flexibility to form 2 : 1 complexes at low palladium loadings. However, at this stage we cannot exclude the possibility that the copolymer precludes coordination of two ligands to a single metal centre and that the active species is actually mononuclear and coordinated by a single ligand. Further studies are clearly required to establish the distribution of 2-pyPPh₂ ligands in these polymers and the composition of the active species. Accepting rapid protonolysis by a proximate pyridyl group to be an integral part of the palladium catalysed alkoxycarbonylation, we reasoned that the introduction of a pyridyl substituent on to the polymer backbone would manifest itself in an increase in catalyst activity. Polyvinylpyridine supported 2-pyPPh₂ **11** was prepared by copolymerisation of 4-vinylpyridine with **3** in the presence of AIBN. Contrary to expectation, replacement of the polystyrene backbone with polyvinylpyridine resulted in a dramatic decrease in activity from 273 to 20 molproduct molPd⁻¹ h⁻¹, even in the presence of a large excess of acid. At this stage we tentatively attribute this decrease in activity to coordination of the polyvinylpyridine matrix to the metal rather than to diffusional limitations or intrusion of the polymer matrix into the coordination sphere of the metal.¹¹ Interestingly, Drent has reported a progressive decrease in catalyst activity with increasing number of pyridyl substituents attached to the phosphine while the number of 2-pyridyl groups had negligible effect on the regioselectivity.² In

this regard, the increase in selectivity to >99.5% with polyvinylpyridine supported 2-pyPPh₂ is remarkable (entry 6). An increase in regioselectivity to >99.95% has previously been achieved by methyl substitution at the 6-position of the 2-pyridyl ring. Since regioselectivity appears to be controlled by steric factors it is tempting to attribute the increase in selectivity associated with polyvinylpyridine supported **11** to a change in the polymer microstructure, possibly as a result of the different swelling capacities in methanol.

In an attempt to glean further information about the polymer composition–catalyst activity/selectivity relationship the performance of polystyrene **12** and polyvinylpyridine **13** supported triphenylphosphine based catalysts was investigated and both were markedly less active than their polystyrene **4** and polyvinylpyridine **11** supported 2-pyPPh₂ counterparts (entries 8 and 9). Moreover, while the selectivity of 80.3% achieved with polystyrene supported triphenylphosphine is similar to that of 81.8% obtained under homogeneous conditions (entry 7), its polyvinylpyridine supported counterpart **13** gave a selectivity >99.5%. This level of selectivity is particularly exceptional for a triphenylphosphine based catalyst and is similar to that obtained with polyvinylpyridine based 2-pyPPh₂ **11**, described above. Thus, while the combination of PPh₃ and a pyridine backbone in **13** does not give high activity it gives a selectivity comparable to that obtained with 2-pyPPh₂ based catalyst systems.



Interest in the selective production of methyl methacrylate prompted us to examine the efficiency of the same catalyst systems in the methoxycarbonylation of propyne, the results of which are listed in Table 1 (entries 11–17). Under standard conditions, the performance of a catalyst mixture generated with **3** was qualitatively similar to that obtained with 2-pyPPh₂. In stark contrast to phenylacetylene, the performance of catalysts generated from polymers **4**, **5** and **10** in the carbonylation of propyne showed a marked dependence on the co-monomer and the tether. For instance, the activity of 1022 molproduct molPd^{−1} h^{−1} obtained with methacrylate-based homopolymer **10** is comparable to that of the homogeneous 2-pyPPh₂ system while the activities obtained with methacrylate-styrene copolymer **5** and the styrene homopolymer **4** are significantly lower, which is likely to be due to better diffusion of the reagents in the more polar polymeric network of **10**. The performance of polyvinylpyridine supported 2-pyPPh₂ **13** and triphenylphosphine **11** were also examined under the same conditions and the activities of 17 and 55 molproduct molPd^{−1} h^{−1}, respectively, correspond to a 20–50 fold decrease in activity compared with that of 1171 molproduct molPd^{−1} h^{−1} for 2-pyPPh₂ under homogeneous conditions. However, catalyst systems based on **11** and **13** both gave a marked increase in

selectivity to >99.5%, which parallels that observed in the methoxycarbonylation of phenylacetylene.

In conclusion, the first insoluble polymer supported 2-pyPPh₂ ligands have been prepared and shown to form highly active and selective catalysts for the alkoxycarbonylation of terminal alkynes. In the case of polyvinylpyridine supported 2-pyPPh₂, very high selectivities were obtained but at the expense of activity. Although the performance of the polystyrene and polymethacrylate based catalysts did not exceed that of the corresponding homogeneous system, in several cases it was very similar and there was no evidence of metal leaching, which renders these immobilized catalysts ideal candidates for multiple recycling in a range of platinum group metal catalysed transformations. Ultimately, we aim to identify robust processible catalysts that can either be extruded or coated onto high surface area substrates for use in a continuous process. Currently, studies are underway to (i) investigate the effect of pyridine ring substitution and basicity on catalyst performance, (ii) expand the range of substrates and reaction types available to these supported 2-pyPPh₂ ligands, (iii) determine the nature and composition of the active species and (iv) systematically modify the co-monomer and the tether to delineate the factors that influence catalyst activity and selectivity.

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