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Polyurea-encapsulated palladium(II) acetate: a robust and recyclable catalyst for use in conventional and supercritical media†

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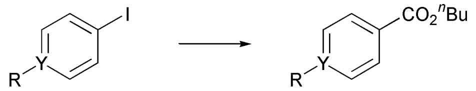
Palladium(II) acetate microencapsulated in polyurea (MC-[Pd]) is an economical and versatile heterogeneous catalyst for a range of phosphine-free cross-coupling reactions in both conventional solvents and supercritical carbon dioxide ($scCO_2$); the catalyst can be recovered by a simple filtration and recycled up to four times.

Reactions leading to the formation of carbon–carbon bonds are central to the assembly of complex organic molecules; the usefulness of palladium chemistry in this regard has assured its place at the forefront of modern synthetic technologies in both research and industrial programmes. These transformations are often mediated by Pd species in the presence of phosphine ligands, and this may result in difficulties associated with the removal of homogeneous material from reaction mixtures. One approach to this problem is to generate 'supported' palladium species, and this tenet has been reflected in the preparation of a range of such variants.[1] The development of an effective phosphine-free supported Pd catalyst suitable for use on a large scale is an attractive prospect with potential for both economic and environmental advantages over solution-phase catalysis. Microencapsulation[2] — a process of entrapping materials in a polymeric coating — provides an alternative approach to supporting transition metal species that may circumvent some of the limitations of conventional polymeric supports. This approach has been exploited in the preparation of polystyrene-encapsulated OsO_4[3] and $Pd(PPh_3)_4$[4] by a coascervation process. Microencapsulated Os and Pd catalysts can also be prepared by an *in situ* interfacial polymerisation approach. As part of a programme concerned with the development of practical and versatile supported catalyst systems, it was decided to investigate the scope and utility of $Pd(OAc)_2$ encapsulated in polyurea in a range of synthetically significant applications — in both conventional and supercritical media. The potential of these materials as catalysts has been demonstrated by their efficacy in Suzuki-type couplings.[5] Extension of these preliminary synthetic studies in both conventional solvents and $scCO_2$ to encompass other widely applicable transformations is described herein. Initial investigations centred upon carbonylation reactions to prepare aryl esters from commercially available aryl iodides. Treatment of 1-iodo-4-methylbenzene with 3 mol% MC-[Pd] in *n*-butyl alcohol and triethylamine at 90 °C under an atmosphere of carbon monoxide gas afforded butyl 4-methyl benzoate in an excellent 89% isolated yield in 16 h

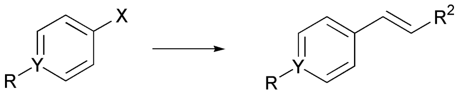
Table 1 Carbonylation reactions with MC-[Pd]



Entry	Transformation[a]		Yield (%)
1	R = Me	Y = C	89
2[b]	R = OMe	Y = C	99
3	R = COMe	Y = C	95
4	—	Y = N	93

[a] Reagents and conditions: 3 mol % MC-[Pd], CO, ^{n}BuOH, Et_3N, 90 °C. [b] See ESI for representative procedure 1, carbonylation reaction.

Table 2 Heck reactions with MC-[Pd]



Entry	Method	Transformation[a]				Yield (%)
1	(i)[b]	R = NO_2	X = Br	Y = C	$R^2 = CO_2{}^nBu$	91
2	(i)	R = NO_2	X = Br	Y = C	R^2 = Ph	93
3	(i)	—	X = I	Y = N	$R^2 = CO_2{}^nBu$	98
4	(i)	R = OMe	X = Br	Y = C	$R^2 = CO_2{}^nBu$	25
5	(ii)[c]	R = H	X = Br	Y = C	$R^2 = CO_2{}^nBu$	99
6	(ii)	R = OMe	X = Br	Y = C	$R^2 = CO_2{}^nBu$	99
7	(ii)	R = F	X = Br	Y = C	$R^2 = CO_2{}^nBu$	75
8	(ii)	R = NO_2	X = Br	Y = C	$R^2 = CO_2{}^nBu$	95
9	(ii)	R = NO_2	X = Cl	Y = C	$R^2 = CO_2{}^nBu$	58[d]

[a] Reagents and conditions: method (i) 2.5 mol % MC-[Pd], IPA, ^{n}Bu$_4$NOAc, 90 °C, olefin component; method (ii) $scCO_2$, 0.4 mol % MC-[Pd], $CH_2 = CHCO_2{}^nBu$, ^{n}Bu$_4$NOAc, 100 °C. [b] See ESI for representative procedure 2, Heck reaction. [c] See ESI for representative procedure 3, Heck reaction in $scCO_2$. [d] Unoptimised.

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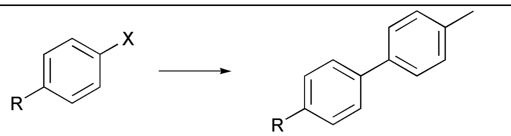
† Electronic supplementary information (ESI) available: representative experimental procedures. See http://www.rsc.org/suppdata/cc/b2/b200677b/

DOI: 10.1039/b200677b

Table 3 Suzuki reactions with MC-[Pd] in $scCO_2$[a]



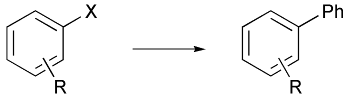
Entry	Transformation[b]		Yield (%)
1	R = H	X = Br	99
2	R = OMe	X = Br	60
3	R = F	X = Br	98
4	R = NO_2	X = Br	78
5	R = NO_2	X = Cl	60

[a] See ESI for representative procedure 4, Suzuki reaction in $scCO_2$. [b] Reagents and conditions: $scCO_2$, 0.4 mol % MC-[Pd], $MePhB(OH)_2$, $^nBu_4NOAc$, 100 °C

(Table 1, entry 1). Inductively coupled plasma (ICP) analysis of the crude reaction mixture (after filtration and drying) indicated 79 ppm Pd (wt/wt), corresponding to 1% leaching of the original Pd content of the capsules. The palladium-containing capsules were removed by a simple filtration and the mixture purified by being passed through a short silica plug (to remove triethylamine residues and salts). The scope of this transformation was established through the generation of a range of substituted aryl esters in high yields, (Table 1). It was decided next to investigate whether these palladium microcapsules could also perform as effective catalysts in Heck type couplings, Table 2. Treatment of 1-bromo-4-nitrobenzene with *n*-butyl acrylate in isopropyl alcohol in the presence of MC-[Pd] (2.5 mol%) and $^nBu_4NOAc$ afforded the requisite unsaturated ester in an excellent 91% yield (Table 2, entry 1). A range of substrates were treated under the same conditions to yield the products in good yields (Table 2, entries 2–4). However, reaction with 4-bromoanisole was less successful, yielding only 25% of the desired product. Under these conditions the crude reaction mixture contained 60 ppm Pd, a loss of 2.8% of the original Pd content of the capsules.

Supercritical carbon dioxide offers real promise as an alternative solvent for organic synthesis,[6] and there has been considerable interest in hydrogenation[7] and Pd-mediated C–C bond forming reactions in this medium.[8] With this in mind, a range of Heck reactions were carried out in $scCO_2$ (Table 2, entries 5–9). Under these conditions, yields were generally higher than in IPA despite a lower catalyst loading. Separation of the catalyst was achieved by simple filtration of the ethyl acetate solution into which the reaction mixture had been vented, demonstrating an advantage of using $scCO_2$; CO_2-soluble products can be extracted from the heterogeneous reaction mixture while the catalyst remains in the reaction cell. After the success of the Heck reactions, a range of Suzuki couplings in $scCO_2$ of tolylboronic acid with aryl halides were examined, which proceeded in yields comparable to those obtained in organic solvents, Table 3.[5] The general synthetic applicability of the MC-[Pd] catalyst was further demonstrated by carrying out a series of Stille coupling reactions between aryl halides and trimethylphenyltin. The coupling of 1-bromo-4-nitrobenzene in an IPA–PhMe mixture was initially attempted, and proceeded smoothly in the presence of $^nBu_4NOAc$ to afford the biaryl derivative in essentially quantitative yield (Table 4, entry 1). The crude reaction mixture was shown to contain 22 ppm Pd, corresponding to leaching of 0.9% of the initial Pd content of the microcapsules. Reactions in the absence of the quaternary ammonium salt were found to be exceptionally slow, leading to very poor conversions. The coupling of deactivated derivatives was also shown to be possible without the use of phosphine ligands; 4-bromoanisole (Table 4, entry 2) was converted to its respective biaryl derivative in 4 h in 88% yield, and 2-bromoanisole was similarly converted in 74% yield in 24 h. The utility of MC-[Pd] in $scCO_2$ is further demonstrated by similar Stille reactions (Table 4, entries 5–8). In these cases, however, yields are generally lower than those observed in conventional solvents. The feasability of recovery and reuse of the catalyst in organic solvents was also examined through a series of sequential Stille couplings of 4-nitrobromobenzene, Table 5. In all cases, the reactions proceeded to completion giving excellent isolated yields, although increases in reaction times were observed.

Table 4 Stille couplings with MC-[Pd]

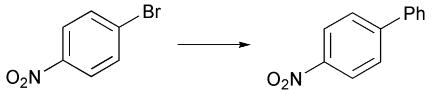


Entry	Method	Transformation[a]		Yield(%)
1	(i)[b]	X = Br	R = *p*-NO_2	99
2	(i)	X = Br	R = *p*-OMe	88
3	(i)	X = Br	R = *p*-F	82
4	(i)	X = Br	R = *o*-OMe	74
5	(ii)[c]	X = Br	R = H	50
6	(ii)	X = Br	R = *p*-OMe	45
7	(ii)	X = Br	R = *p*-NO_2	>34
8	(ii)	X = Cl	R = *p*-NO_2	50

[a] Reagents and conditions: method (i) 2.5 mol % MC-[Pd], IPA–PhMe (1:1, v/v), $^nBu_4NOAc$, Me_3SnPh, 90 °C; method (ii) $scCO_2$, 0.4 mol % MC-[Pd], Me_3SnPh, 100 °C. [b] See ESI for representative procedure 5, Stille reaction. [c] See ESI for representative procedure 6, Stille reaction in $scCO_2$

Table 5 Stille couplings: recycling experiments[a]

Substrate:



Run	1	2	3	4
Yield (%)	99	98	99	97
Time/h	3	4.5	12	24

[a] Reagents and conditions: 2.5 mol % MC-[Pd], IPA/PhMe (1:1, v/v), Me_3SnPh, nBu_4NOAc, 90 °C.

In this communication it has been demonstrated that $Pd(OAc)_2$ encapsulated in polyurea is an accomplished catalyst for cross-coupling reactions in both conventional and supercritical media that can be removed simply and effectively from reaction mixtures by a filtration process. The flexibility of the encapsulation process suggests the prospect of a more rational design tailored to specific applications.

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