The use of palladium on porous glass for catalytic coupling reactions

Jintong Li, Albert W.-H. Mau and Christopher R. Strauss*

CSIRO Division of Molecular Sciences, Private Bag 10, Clayton South MDC, Victoria 3169, Australia

Palladium on porous glass is a useful heterogeneous catalyst for liquid phase organic coupling reactions which can be carried out in the presence of air, without the need for solubilizing and activating ligands.

Catalysts of palladium, its complexes and its salts, are well recognized for activation of C–H bonds towards coupling reactions.[1–3] In this regard, the Heck reaction of an aryl or vinyl halide with an alkene in the presence of palladium derivatives has been the subject of intensive study and there is growing interest in synthetic transformations of terminal alkynes *via* homo- or hetero-couplings of the Glaser, Eglington or Chodkiewicz–Cadiot type.[4–6]

However, commercial development, particularly of Heck reactions, has not progressed as rapidly as could have been expected, most likely because of low turnover numbers and low turnover frequencies.[7] The susceptibility of palladium catalysts to poisoning also necessitates the use of relatively large amounts (1–5 mol%) of expensive metal to ensure acceptable conversions.[8] Attempts at overcoming these disadvantages have involved the use of organopalladium complexes, usually containing phosphine ligands, as homogeneous catalysts.[1–3] Although such complexes can be difficult to separate from product mixtures and to recover from reaction media,[9] some recent success has been obtained with methods employing homogeneous two-phase catalysis.[10] Nonetheless, many phosphine ligands are thermally unstable, even at temperatures as low as 120 °C,[11] so maximum reaction temperatures are limited. In some cases, aryl groups emanating from degraded phosphines can react with olefinic starting materials, thereby affecting the course of the reaction.[12,13] Benefits of phosphine-free palladium catalysts have been discussed.[14]

In ongoing research into the development of technologies for environmentally benign chemistry,[15] we have investigated palladium metal on porous glass tubing as a catalyst for chemical syntheses. The catalyst may be similar to the membrane developed for hydrogen separation by Uemiya *et al.*,[16] and analogous to the platinum on porous glass used by Sun and Khang for dehydrogenation of cyclohexane.[17] Although such catalysts do not appear to have been employed for coupling reactions their potential advantages, including mechanical and thermal stability, solvent resistance, reusability, longevity, and obviation of air- and temperature-sensitive ligands have strong appeal.

Our *ca.* 0.18% palladium on porous glass tubing could be used for reactions conducted continuously or batchwise. It offered resistance to oxidative deterioration and could be re-used several times for repeat or different reactions. Examples, mostly carried out in the presence of air, with either conventional heating or under microwave irradiation in a novel pressure-tight batch reactor (MBR),[18] are compiled in Table 1.† Turnover numbers for entries 1–8 in this table were calculated from single, non-exhaustive reaction runs and have been compiled to show that the palladium was catalytic. For the Heck coupling of 4-bromoacetophenone with styrene, when the same sample of catalyst was re-used several times, or when the molar ratio of catalyst to reactants was substantially decreased (*e.g.* 0.02 mol% Pd was used for entry 9, Table 1), the turnover

Table 1 Example reactions and conditions (*N*,*N*-dimethylacetamide as solvent)

Entry	Starting material(s)	*T*/°C	*t*/h	Major product(s)	Conversion (%)	Turnover number
1	$PhI + CH_2{=}CH{-}CH_2OH$	120[a]	3	$PhCH_2CH_2CHO$ + $PhCH{=}CHCHO$ + by-products (52 : 30 : 18)	99	> 100
2	$PhI + PhCH{=}CH_2$	180[a]	1.5	*trans*- + *cis*-$PhCH{=}CHPh$ + $(Ph)_2CH{=}CH_2$ (83 : 1 : 16)	100	> 100
3	PhI + phenylacetylene	100[b]	88	1,2-diphenylacetylene	95[c]	> 100
4	4-bromobenzaldehyde + phenylacetylene	100[b]	24/72/96	4′-formyl-1,2-diphenylacetylene	79[c]/86[c]/100[c]	> 100
5	4-bromoacetophenone + phenylacetylene	140[b]	12/100	4′-acetyl-1,2-diphenylacetylene	55[c]/87[c]	> 100
6	4-bromoacetophenone + 1-hexyne	100[a]/ 140[a]	6/2	1-(4′-acetyl)phenylhex-1-yne + by-products[d] (51 : 49)	16/73	*ca.* 100
7	2-bromopyridine + phenylacetylene	140[b]	48/100	2-(2-pyridyl)-1-phenylacetylene	55[c]/83[c]	*ca.* 100
8	phenylacetylene	150[b]	48	1,4-diphenylbuta-1,3-diyne + homo-addition product (93 : 7)	71	*ca.* 100
9	4-bromoacetophenone + styrene	180[e]	12	*trans*- + *cis*-4′-acetyl-1,2-diphenylethylene + 1-(4-acetylphenyl)-1-phenylethylene (91 : 2 : 7)	98	4000

[a] Carried out in air, with the MBR. [b] Carried out in air, with conventional heating. [c] 1,4-diphenylbuta-1,3-diyne and a homo-addition product (M_w 204) of phenylacetylene were present. [d] Some of these were formed by addition of hex-1-yne to the product. [e] Conventional heating, under argon.

numbers were an order of magnitude greater than the other values shown in Table 1.

The regioselectivity of Heck reactions was consistent with Heck's observation that terminal alkenes yield about $80:20$ mixtures of 1- and 2-arylated alkenes when there are no major steric influences (see entries 2 and 9, Table 1).[3] Also in agreement with previous findings,[19] Heck reaction of iodobenzene with allyl alcohol afforded 3-phenylpropionaldehyde as the major product (entry 1, Table 1). However, *trans*-3-phenylprop-2-enal was also produced and in greater abundance than the expected regioisomer 2-phenylpropionaldehyde.[3] To our knowledge, this olefinic aldehyde has not been reported from the same reactants under Heck conditions. Air present during the reaction may have played a role, an aspect which will require further investigation.

Similarly with Heck reactions, internal alkynes can be obtained by coupling of aryl iodides or bromides with terminal acetylenes under palladium catalysis.[5] However, typical requirements for high amounts of catalyst (1–5 mol% Pd) and coaddition of copper salts (also 1–5 mol% in Cu) can diminish the industrial viability of such procedures.[8] New moisture-stable phosphapalladocycles, without copper salts, recently afforded a high yielding coupling of 4-bromoacetophenone with phenylacetylene, albeit under a single set of satisfactory conditions. When alternative starting aryl halides and alkynes were used, reaction either did not proceed or was only moderately successful in most cases.[8]

With palladium on porous glass, neither copper salts nor activating ligands were necessary. Conversions for the coupling of phenylacetylene with iodobenzene and with 4-bromobenzaldehyde were nearly quantitative (entries 3 and 4, respectively, Table 1) and were satisfactory for phenylacetylene with 4-bromoacetophenone (entry 5, Table 1) and 2-bromopyridine (entry 7, Table 1). Although several of these results were comparable with those of Herrmann *et al.*, the coupling of 4-bromoacetophenone with phenylacetylene in dimethylacetamide (DMA) with NaOAc as base and also the reaction of this ketone with hexyne proceeded with palladium on porous glass (see entries 5 and 6, Table 1) where it had failed with the phosphapalladocycles.[8]

Homocoupling of phenylacetylene[20] was apparent in all reactions involving this alkyne, so not surprisingly, 1,4-diphenylbuta-1,3-diyne was formed quite efficiently in the absence of other reactants (entry 8, Table 1). Thermal addition products of (M_w 204) were also formed in relatively low amounts in all reactions involving phenylacetylene.

The above results show that palladium on porous glass is a useful catalyst for synthetic coupling reactions, and suggest that it could have applications in other reactions catalysed by palladium, *e.g.* dehydrogenation[17] and hydrogenation.

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Footnotes

* E-mail: chris.strauss@molsci.csiro.au

† Prewashed porous glass tubing (7 mm o.d., 4.8 mm i.d. tubing with 250 $m^2\ g^{-1}$ internal surface area, 28% porosity; 2.54 g) was allowed to stand overnight in an aqueous solution (50 ml) of $[Pd(NH_3)_4]Cl_2$, containing 110 ppm in palladium. It was then removed, washed three times with deionised water and immersed in a solution comprising $NaBH_4$ (2.0 g) in deionised water (100 ml), at room temperature for up to 5 h. In a typical experiment, a mixture of 4-bromoacetophenone (5 mmol) and phenylacetylene (8 mmol) in *N*,*N*-dimethylacetamide (50 ml) containing NaOAc (8 mmol) and 0.18% Pd on porous glass (2.54 g glass; 0.043 mmol Pd) was heated with stirring for 100 h in air at 140 °C. At regular intervals, samples were withdrawn for analysis by GC and GC–MS. See entry 5, Table 1.

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