Dithio palladium modified silicas—New heterogeneous catalysts for Suzuki cross-coupling reactions

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Abstract

Novel heterogeneous silica supported 1,2-bis(ethylthio)ethane palladium and 1,2-bis(ethylthio)propane palladium catalysts are reported. Applied to Suzuki coupling chemistry these catalysts are very effective, reusable and resist leaching at room temperature in isopropanol or in hot xylene.
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1. Introduction

Many palladium complexes as well as supported palladium complexes have been investigated as homogeneous and heterogeneous catalysts, respectively, for Suzuki C–C bond forming reactions. This chemistry is compatible with a large variety of functional groups. The literature covering this area has very recently been reviewed and an extensive range of reaction conditions has been explored [1]. The challenges for the heterogeneous systems are linked to maximising activity while minimising the palladium requirement and optimising ligand design to prevent palladium leaching. To this end many different types of immobilized ligands have been explored to bind, for example, palladium chloride or palladium acetate for use in heterogeneous catalytic Suzuki chemistry. The list of silica-immobilized palladium binding ligands includes Schiff bases [2], *N*-heterocyclic carbene [3], polyamines or pyridine [4] and imadazolylpropyl [5]. Of particular relevance to this paper are studies on silica-immobilized sulfur containing ligands. Shimizu and co-workers reported that silica supported mercaptopropyl palladium is virtually resistant to leaching of palladium during Suzuki and Heck coupling [6]. Using similar catalysts Crudden confirmed minimal leaching of palladium by three-phase tests

and analysis of hot filtrates [7]. We recently reported on silica-immobilized palladium ethylthioglycolate catalysts for both Heck and Suzuki coupling [8]. We found that this system was effective and recyclable with no evidence of palladium leaching. The effective palladium binding was attributed to the presence of sulfur in the thioglycolate ligand. In this paper we report on new silica immobilized di(ethylthio)ethane and di(ethylthio)propane palladium catalysts having two sulfur donor atoms in the immobilized ligands to enhance binding through sulfur coordination. Catalyst synthesis and conditions for use in Suzuki coupling chemistry at both room temperature and 110 °C are reported.

2. Results and discussion

In this paper we report on the synthesis, characterisation, and catalytic activity of some functionalised silica materials derived from 1,2-bis(trimethoxysilylethylthio)ethane **1** and 1,2-bis(trimethoxysilylethylthio)propane **2**. The silica supported derivatives, silica~$(CH_2CH_2S(CH_2)_2SCH_2CH_2)$~silica **3** and silica~$(CH_2CH_2S(CH_2)_3SCH_2CH_2)$~silica **4** were formed from the trimethoxysilyl compounds by grafting to commercial silica with pore size 60 Å (see Scheme 1). Post-modification of **3** and **4** with palladium acetate gave materials **5** and **6** with likely structures shown in Scheme 1. Trimethyl- and triphenylsilyl analogues of **1** and **2**, 1,2-bis(trimethylsilylethylthio)ethane, **7** and 1,3-bis(triphenylsilylethylthio)propane, **8**, were also prepared to aid confirmation of NMR assignments of the solid phase

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Scheme 1.
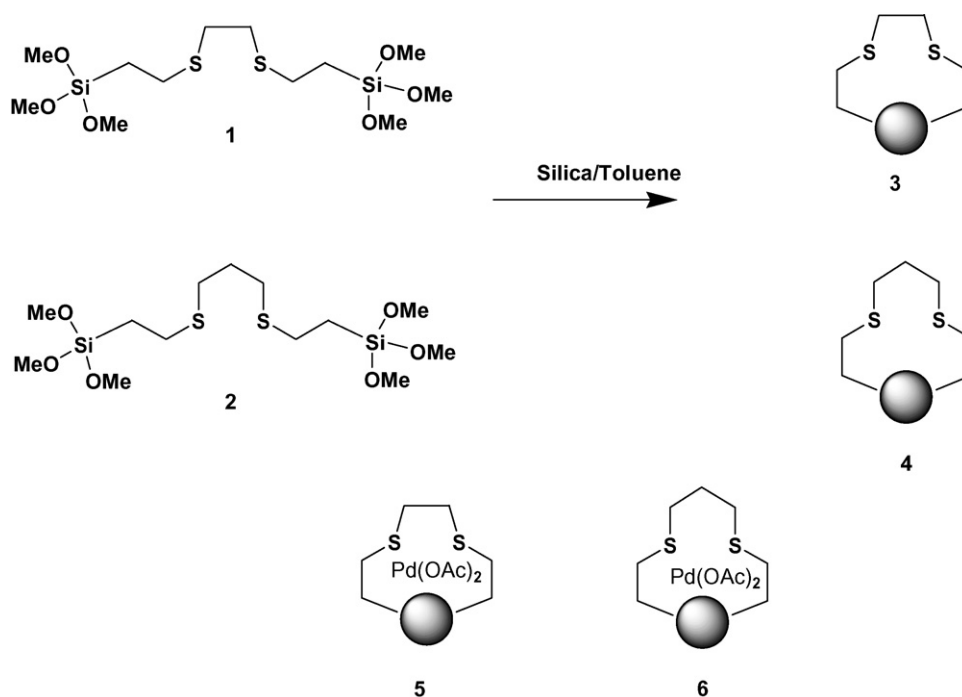
immobilized heterogeneous systems. Immobilisation was confirmed by solid state NMR, ^{13}C (ligand resonances observed) and ^{29}Si (T and Q resonances observed). The functional group loadings were estimated from sulfur analysis and the Pd loading by ICP-OES after digestion.

Sulfur analysis indicated that the grafted material **3** had a ligand, Si(CH$_2$CH$_2$S(CH$_2$)$_2$SCH$_2$CH$_2$)Si, loading of 0.6 mmol g^{-1} while **4** had Si(CH$_2$CH$_2$S(CH$_2$)$_3$SCH$_2$CH$_2$)Si loading 0.5 mmol g^{-1}. The supported Pd catalysts used in this work were prepared by stirring the grafted materials **3** or **4** with palladium acetate in THF at room temperature for 24 h. Deep orange coloured palladium acetate loaded materials **5** and **6** were obtained.

The PdS$_2$C$_2$ and PdS$_2$C$_3$ ligation indicated in the scheme for **5** and **6** is featured in a large number of palladium complexes, for example see [9] or [10], listed on the Cambridge Crystallographic Database. The uptake of palladium acetate by **3** and **4** is extremely rapid. The measured Pd loadings were 0.38 mmol g^{-1} **5** and 0.46 mmol g^{-1} **6**. The surface areas of the materials decreased from ∼380 m^2/g in **3** and **4** to ∼200 m^2/g in **5** and **6** after treatment with palladium acetate which is consistent with similar palladium acetate uptake. The ^{13}C CPMAS spectra show line broadening of all resonances in **5** and **6** relative to **3** and **4**, respectively (exemplified for **4** and **6** in Fig. 1). A new peak at ∼90 ppm in the Pd acetate loaded material may be assigned to the quaternary carbon of bidentate acetate.

Materials **5** and **6** were assessed as heterogeneous catalysts for a range of Suzuki coupling reactions under two different sets of reaction conditions. The results are given in Table 1.
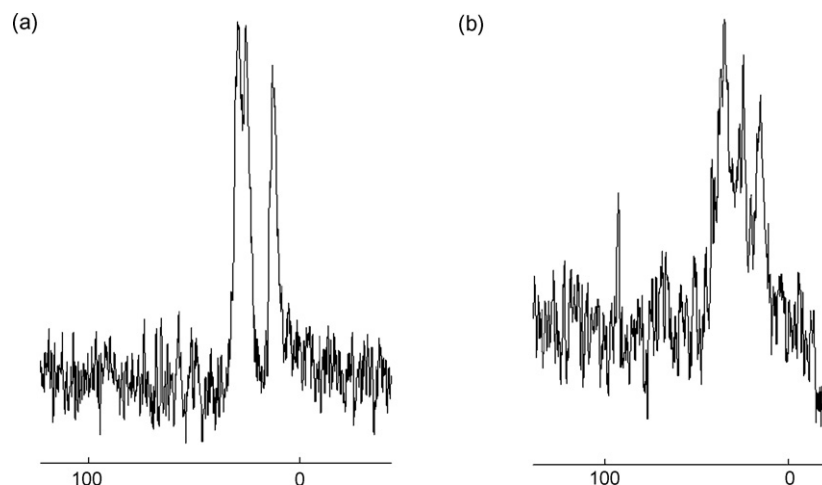

Fig. 1. ^{13}C CPMAS NMR of (a) **4** and (b) **6**.

Table 1
Suzuki reactions

R—⟨C6H4⟩—Br + ⟨C6H5⟩—B(OH)₂ →(K₂CO₃, Xylene, 110 °C, 1.5 mol% Pd **or** NaOBu^t, Pr^{i}OH 25 °C, 3 mol% Pd) ⟨C6H5⟩—⟨C6H4⟩—R

Entry	Substrate	% Conversion[a] (**5** cycle 1, 2, 3 (h); **6** cycle 1, 2, 3 (h))	% Conversion[b] (**5** cycle 1, 2, 3 (h); **6** cycle 1, 2, 3 (h))
1	⟨C6H5⟩—Br	99, 99, 99 (2); 99, 99, 99 (2)	98, 95, 95 (6); 99, 99, 95 (6)
2	MeO—⟨C6H4⟩—Br	99, 97, 97 (2); 99, 98, 95 (2)	95, 94, 94 (6); 99, 99, 99 (6)
3	Me—⟨C6H4⟩—Br	99, 90, 90 (7); 98, 90, 90 (7)	88, 86, 88 (6); 99, 99, 99 (6)
4	Cl—⟨C6H4⟩—Br	99, 96, 90 (7); 99, 99, 96 (7)	76, 76, 74 (6); 99, 90, 87 (6)
5	MeO—⟨C6H4⟩—Cl	–; 6 (24)	5 (24); 4 (24)
	⟨pyridyl⟩—Br	–; 99 (2)	

[a] Taken, 1.5 mmol phenylboronic acid, 1.0 mmol aryl halide, 1.5 mmol K₂CO₃, 50 mg **5** or **6**, 1.9 mol% Pd and 2.3 mol%, respectively, 7 mL xylene. Conversion determined by GC all and NMR 4-bromoanisole and 4-bromotoluene.

[b] Taken 1.5 mmol phenylboronic acid, 1.0 mmol aryl halide, 1.2 mmol NaOBu^t, 100 mg catalyst **5**, 3.8 mol% Pd or 70 mg catalyst **6** 3.2 mol% Pd, 4 mL isopropanol. Conversion determined by ¹H NMR or GC.

The choice of conditions used, hot xylene and potassium carbonate as base, for the first set of experiments with catalysts **5** and **6** was based on those frequently reported for both homogeneous and heterogeneous catalysed Suzuki coupling reactions and those we previously employed for similar reactions with immobilized palladium glycolate catalysts [8]. Under these conditions close to quantitative conversions were observed for the Suzuki reactions with aryl bromides. The catalysts could be recycled without loss in activity. This was typically accomplished by removal of supernatant liquid from the catalyst followed by addition of fresh substrates, solvent and base. A filtration protocol, wherein fresh base was added to the hot filtrate, was applied to the reaction with bromoanisole as substrate, 50 min into the run. This resulted in no further conversion which is indicative of negligible palladium leaching. The apparent excess of Pd free sulfur ligand sites in the materials should facilitate Pd retention. The catalyst is clearly more active and activity more effectively preserved between runs with activated bromide substrates under these conditions (conversion is slower for entries 3 and 4). Chloroanisole was not converted. There are no major differences in activity between the catalysts **5** and **6** under these conditions.

The second set of experiments using **5** and **6** were performed at room temperature using isopropanol in place of xylene and sodium *tert*-butoxide as base. These reducing conditions had previously been used by Nolan et al. in studies involving homogeneous palladium carbene catalysts [11]. High and recyclable conversions were achieved with **6** for aryl bromide substrates at room temperature under these conditions while **5** was a little more sluggish particularly with less activated substrates. This is in contrast to the reactions carried out in hot xylene where the cat-

alysts showed very similar activity. The slightly lower Pd loading and surface area and slightly more constrained PdS₂C₂ coordination environment in **5** may be more limiting at room temperature. The catalysts were recycled without significant drop in activity. Conversion to the coupled product ceased when the reactions were filtered after 1 h (and fresh base added). This is indicative of negligible Pd leaching. Once again chloroanisole was not converted. Cesium carbonate proved an effective alternative to the *tert*-butoxide base for bromotoluene under these conditions although other bases including triethylamine and sodium acetate were less effective.

In terms of mechanism, the reaction conditions utilizing isopropanol are typically reducing for Pd(II) so that a Pd(0)/(II) couple is envisaged for the cycle. In contrast the reactions carried out in xylene are not obviously reducing for Pd(II) and so are more likely to proceed by the Pd(II)/(IV) couple. Further studies on the catalytic materials are in hand to probe these mechanistic aspects. The compounds **1** and **2** can also be processed by sol-gel routes with TEOS to give very high loaded silica supported di(ethylthio)ethane and propane products or they may be processed alone to give the organobridged polysilsesquioxanes. Details and properties of these materials will be published in due course.

3. Experimental

3.1. General information

All reagents used were purchased from Aldrich, Avocado or Lancaster and were used without further purification, unless

otherwise stated. Silica was supplied by Grace. Instruments: solution state ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL JNM-EX270 spectrometer, solid state NMR spectra were recorded on a Bruker AMX 400 MHz (^{29}Si SPE MAS, frequency 119.2 MHz, spinning speed 12 kHz; 1 min recycle delay, with 2 μs ∼ 45° pulse; ^{13}C CP MAS; frequency 150.9 MHz, spinning speed 10 kHz, 1 ms contact time, 5 s delay, 90° pulse for 3.5 μs). Mass spectra were recorded on a Micromass QuattroII mass spectrometer. Surface areas were measured using a Micromeritics Flowsorb II 2300 single point surface area analyser.

3.2. 1,2-Bis(trimethoxysilylethylthio)ethane 1

To trimethoxyvinylsilane (67 mL, 0.44 mol) was added 1,2-ethanedithiol (20 mL, 0.2 mol). The mixture was stirred at room temperature for 1 h. The volatiles were evaporated under reduced pressure at 100 °C giving the colourless oil **1**. ^{1}H NMR (CDCl$_3$) δ_H: 0.76 (4H, t, J = 4.2, SiCH_2), 2.51 (8H, m, CH_2), 3.37 (18H, s, OMe); ^{13}C NMR (CDCl$_3$) δ_C: 10.5 (SiCH_2), 25.9 (CH_2S), 31.6 (SCH_2CH_2S), 50.3 (OCH_3); ^{29}Si NMR (CDCl$_3$) δ_{Si}: −49.06.

3.3. 1,3-Bis(trimethoxysilylethylthio)propane 2

To trimethoxyvinylsilane (67 mL, 0.44 mol) was added 1,3-dithiopropane (20 mL, 0.2 mol). The mixture was stirred at room temperature for 1 h. The volatiles were evaporated under reduced pressure at 100 °C to give the colourless oil **2** (79 g, 99%). ^{1}H NMR (CDCl$_3$) δ_H: 0.77 (4H, t, J = 8.1, SiCH_2), 1.63–1.69 (2H, m, CH_2), 2.45 (8H, m, CH_2), 3.38 (18H, s, OCH_3); ^{13}C NMR (CDCl$_3$) δ_C: 10.5 (SiCH_2), 25.9 (CH_2S), 29.1 (S$CH_2CH_2CH_2$S), 30.6 (S$CH_2CH_2CH_2$S), 50.4 (OCH_3); m/z (ESI): 422 (M$^+$, 100%), 274.1 (22%), 138.1 (49%). ^{29}Si NMR (CDCl$_3$) δ_{Si}: −45.04. FAB-MS (m/z): [M+NH$_4$]$^+$ Calcd for C$_{13}$H$_{32}$O$_6$S$_2$Si$_2$, 422.1517; found, 422.1515; m/z (%): 422 (M$^+$, 100), 274.1 (22), 138.1 (49)

3.4. ∼(CH$_2$CH$_2$S(CH$_2$)$_2$SCH$_2$CH$_2$)∼silica 3

A mixture of compound **1** (12 g, 28 mmol) and silica (40 g) in toluene (100 mL) was stirred and refluxed for 8 h. After cooling the mixture was filtered, washed with methanol and then dried for 2 h to give a white powder **3**. ^{13}C NMR (CP MAS) δ_C: 13 (SiCH_2), 26 (CH_2S), 33 (SCH_2CH_2S); ^{29}Si NMR (MAS) δ_{Si} −64.1, −68.3, −86.3, −97.8, −106.6. Specific surface area 370 m^2/g. %S found = 3.6%.

3.5. ∼(CH$_2$CH$_2$S(CH$_2$)$_3$SCH$_2$CH$_2$)∼silica 4

A mixture of compound **2** (6 g, 14.8 mmol) and silica (20 g) in toluene (70 mL) was stirred and refluxed for 8 h. After cooling the mixture was filtered, the solid residue was washed with methanol and then dried to afford a white powder **4**. ^{13}C NMR (CP MAS) δ_C: 13 (SiCH_2), 26 (CH_2S), 29 (S$CH_2CH_2CH_2$S). Specific surface area 380 m^2/g. %S found = 3.29%.

3.6. 3-Pd(OAc)$_2$ 5 and 4-Pd(OAc)$_2$ 6

A solution of palladium acetate (0.16 g, 0.7 mmol) in THF (50 mL) was added to material **3** or **4** (1 g). The mixture was stirred overnight and the colourless liquid was filtered from an orange solid. The solid was washed well with THF and then dried under reduced pressure 60 °C at 0.01 mm of Hg giving **5** or **6**. The palladium content was measured by ICP after the materials were digested.

5 ^{13}C NMR (CP MAS) δ_C: 14 (SiCH_2), 25 (CH_2S), 38 (SCH_2CH_2S); Pd loading 0.38 mmol/g. Specific surface area 202 m^2/g. **6** ^{13}C NMR (CP MAS) δ_C: 15 (SiCH_2), 26 (CH_2S), 35 (S$CH_2CH_2CH_2$S), 93 (CH_3CO_2); ^{29}Si NMR (MAS) δ_{Si}: −70.5, −106.9, −116.7. Pd loading 0.46 mmol/g. Specific surface area 194 m^2/g.

3.7. 1,2-Bis(trimethylsilylethylthio)ethane 7

To trimethyl(vinyl)silane (0.73 g, 7.32 mmol) was added 1,2-ethanedithiol (0.23 g, 2.49 mmol) and a few drops of di-tert-butylperoxide was added to the reaction mixture at 2 h intervals for the first six hours. The reaction was stirred for 24 h at 70 °C. The colourless oil was purified *via* flash column chromatography using ethyl acetate:petroleum ether (1:9) to yield (0.70 g, 96%). IR ν (cm^{-1}): 724, 839, 1248; ^{1}H NMR (CDCl$_3$) δ_H: 0.02 (18H, s, SiCH_3), 0.87 (4H, bs, SiCH_2), 2.60–2.89 (8H, m, CH_2); ^{13}C NMR (CDCl$_3$) δ_C: −1.7 (SiCH_3), 17.5 (SiCH_2), 27.8 (CH_2S), 31.9 (SCH_2CH_2S); ^{29}Si NMR (CDCl$_3$) δ_{Si}: 1.32; FAB-MS (m/z): [M+H]$^+$ Calcd for C$_{12}$H$_{30}$S$_2$Si$_2$, 295.1400; found, 295.1403; m/z (%): 295 (M$^+$, 70), 161 (30), 90 (100), 73 (12).

3.8. 1,2-Bis(triphenylsilylethylthio)propane 8

To triphenylvinylsilane (0.5 g, 1.75 mmol) was added 1,3-dithiopropane (95 mg, 0.088 Ml, 0.88 mmol) and a few drops of di-tert-butylperoxide was added to the reaction mixture at 2 h intervals for the first six hours. The reaction was stirred for 24 h at 70 °C. The colourless oil was purified by flash column chromatography, ethyl acetate:petroleum ether (40–60 °C) (1:9), to give a white solid (0.55 g, 92 %); mp: 140–142 °C; IR ν (cm^{-1}): 721, 1111, 1377, 1461; ^{1}H NMR (CDCl$_3$) δ_H: 1.69–1.78 (6H, m, SiCH_2), 2.54–2.68 (8H, m, CH_2), 7.25–7.50 (30H, m, Ar-H); ^{13}C NMR (CDCl$_3$) δ_C: 14.5 (SiCH_2), 27.6 (CH_2S), 29.3 (CH_2S), 30.8 ($CH_2CH_2CH_2$), 128.1 (Ar-C), 129.8 (Ar-C), 134.3 (Ar-C), 135.6 (Ar-C); ^{29}Si NMR (CDCl$_3$) δ_{Si}: −11.77. EI/CI-MS m/z (%): 681 (M$^+$, 8), 603 (90), 529 (60), 393 (100). Anal Calcd for C$_{43}$H$_{44}$O$_2$S$_2$Si$_2$: C, 75.83; H, 6.51. Found: C, 72.87; H, 6.43.

3.8.1. Leaching tests

A sample from the Suzuki reaction with bromoanisole was taken after 50 min for evaluation and the remainder of the hot supernatant syringe filtered into a clean reaction flask. Further solvent and base was added to the filtrate and the reaction continued in the absence of catalyst for a further 6 h. Conversion was found to be 50% after 50 min. Analysis showed no further conversion following this hot filtration.

For the reactions carried out in isopropanol at room temperature the reaction mixture was filtered after 1 h. Further solvent and base was added to the filtrate and the reaction continued in the absence of catalyst for a further 3 h. Conversion was found to be 43% at 60 min. Analysis showed no further conversion following this filtration.

Acknowledgements

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