

Palladium ethylthioglycolate modified silica—a new heterogeneous catalyst for Suzuki and Heck cross-coupling reactions

Mohammed Al-Hashimi^a, Alice C. Sullivan^{a,*}, John R.H. Wilson^b

^a School of Biological and Chemical Sciences, Queen Mary, University of London,
Mile End Road, London, E14 4NS, UK

^b PhosphonicS Ltd., 114 Milton Park, Oxford, OX14 4SA, UK

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Abstract

A novel heterogeneous silica supported palladium ethylthioglycolate catalyst which is active and recyclable for Suzuki and Heck reactions is reported.

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1. Introduction

Palladium catalysed Heck or Suzuki C–C forming reactions using aryl bromides as one of the substrates are among the most versatile reactions for organic synthesis since they are compatible with a large variety of functional groups. Many palladium complexes have been investigated as homogeneous catalysts and many supported palladium complexes as heterogeneous catalysts for these reactions. An extensive range of reaction conditions have been explored and the literature on this area has very recently been reviewed [1]. Of particular relevance to this paper are the silica supported ligands that have been employed to immobilise palladium chloride or palladium acetate for solid phase catalytic reactions. Some examples of these from the recent literature are listed as follows. Clark and Paul demonstrated structure activity relationships for silica supported Schiff base palladium catalysts in Suzuki reactions [2]. Karimi and Enders reported a series of Heck coupling reactions between iodo or bromo benzenes and acrylates catalysed by silica immobilised *N*-heterocyclic carbene palladium dichloride complexes [3]. Khinast reported on Suzuki coupling catalysed by palladium chloride coordinated to propylamine-, propylethylenediamine- or ethyl pyridine-functionalised silicas [4]. Imidazolyl ligated

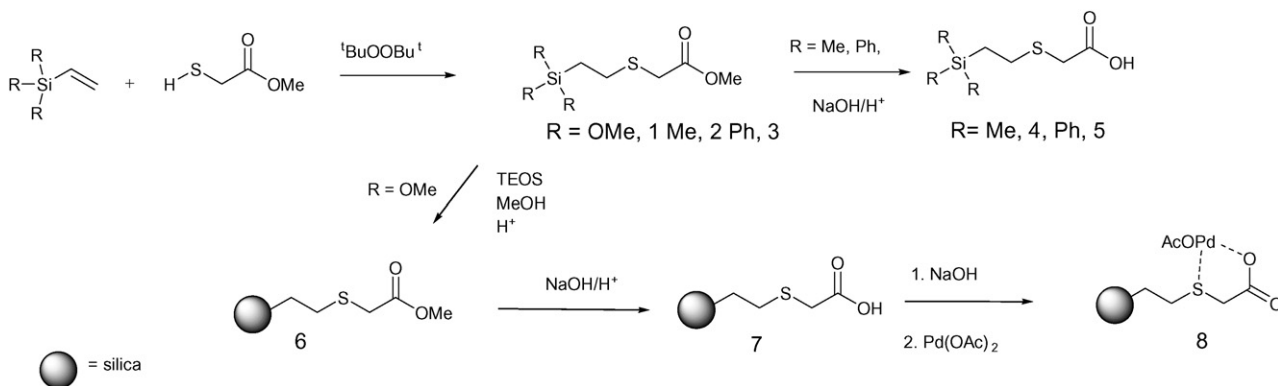
palladium chloride in imidazolylpropyl functionalised silica was found to be active and reusable for both Suzuki and Heck chemistries [5]. Supported polyamidoamine dimethylpalladium dendrimers were found to be active and reusable catalysts for Heck chemistries [6]. Supported oxime carbapalladacycle catalyst are active for Suzuki cross-coupling [7]. In studies on sulfur containing ligands Shimizu and co-workers showed that silica supported mercaptopropyl palladium is active for Suzuki and Heck coupling and virtually resistant to leaching of palladium [8] while using similar catalysts Crudden et al. confirmed minimal leaching of palladium by three-phase tests and analysis of hot filtrates [9]. Herein we report on a new sulfur containing silica immobilized palladium catalyst and initial studies of its application to Suzuki and Heck chemistries.

2. Results and discussion

In this paper, we report on the synthesis, characterisation, and catalytic activity of some novel silica supported thioglycolate materials derived from hydrolytic polycondensation of trimethoxysilylethylthio(methyl)glycolate **1** with TEOS (see Section 3 for preparation of compound **1**). The corresponding carboxylic acid, silica~CH₂CH₂SCH₂CO(OH) and acetate, silica~CH₂CH₂SCH₂CO(ONa), were obtained by post modification of the solid supported ester silica ~CH₂CH₂SCH₂CO(OMe), as outlined in Scheme 1 below and described in Section 3.

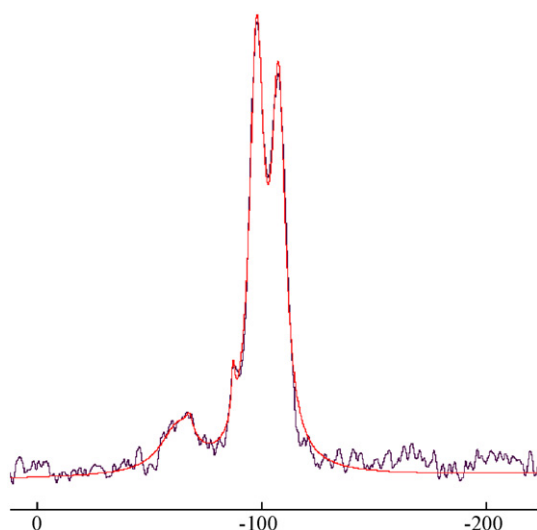
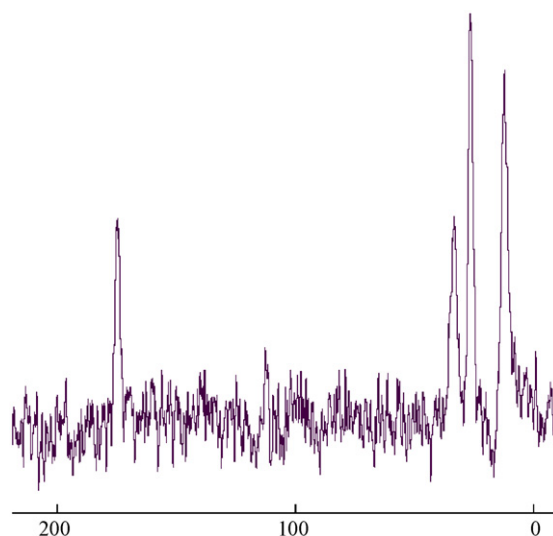
* Corresponding author.

E-mail address: a.c.sullivan@qmul.ac.uk (A.C. Sullivan).



Scheme 1.

Uptake of palladium acetate from the sodium thioglycolate to give palladium ethylthioglycolate with presumed structure **8** is extremely rapid as indicated by the fast colourisation of the solid in contact with the palladium acetate solution. The surface immobilisation process is very likely assisted by coordination to sulfur in addition to acetate (coordination to both sulphur and acetate is observed in molecular palladium thioglycolate complexes [10]). The molecular compounds trimethyl- and triphenylsilylethylthioglycolic acids and their methyl esters, $R_3SiCH_2CH_2SCH_2CO(OH)$ and $R_3SiCH_2CH_2SCH_2CO(OMe)$ $R = Me, Ph$, were prepared (Scheme 1) to confirm NMR assignment of the supported compounds. A combination of methods was used to characterise the functionalised silica materials including solid state ^{13}C and ^{29}Si NMR (see Section 3). Examples of solid state spectra are shown in Figs. 1–3. The $T:Q$ ratio (that is ratio of functional group silicon:framework silicon) was obtained from the fitted [11] ^{29}Si MAS NMR spectrum (Fig. 1) whereby 12.4% T and 87.6% Q was found giving $T:Q$ of 1:7 and a T loading of 1.6 mmol g^{-1} . The elemental analysis of **7** gave 4.06% S implying a T loading of 1.3 mmol g^{-1} from which the $T:Q$ ratio of 1:10 is suggested (where average formulae are based on the fully condensed system). The latter ratio is consistent with the mol ratio of T and Q

Fig. 1. ^{29}Si MAS NMR of **7** with Gaussian fitting.Fig. 2. ^{13}C CPMAS NMR of **7**.

precursor reagents taken (1:10) and is probably a more accurate estimation of the T loading. The Pd loading, 1.1 mmol g^{-1} , was established using atomic absorption (see Section 3) and the harsh conditions used to liberate the Pd reflects the high ligand affinity for the metal. Surface areas (m^2/g) of the materials changed from 494, **6** to 630, **7** to 340, **8**, consistent with the conversion of

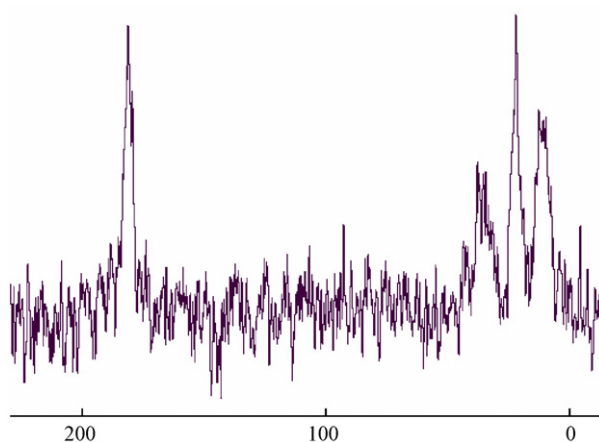
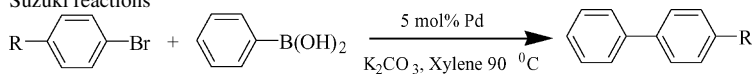
Fig. 3. ^{13}C CPMAS NMR of **8**.

Table 1
Suzuki reactions



Substrate ^{a,c}	Time/h	%Conversion ^b (cycle 1, cycle 2, cycle 3)
	2.0	99, 99, 90
	1.5	99, 99, 90
	2.5	–, –, 99
	1.5	97, 90, 90
	4.5	–, 97, –
	1.5	97, 90, 90
	2.5	–, 94, –

^a Taken, 1.5 mmol phenylboronic acid, 1.0 mmol aryl halide, 1.5 mmol K₂CO₃, 50 mg catalyst, 7 mL xylene.

^b Conversion determined by GC all and NMR 4-bromoanisole and 4-bromotoluene.

^c Chloroanisole 47 h 99%.

ester to acid and subsequent introduction and accommodation of a PdOAc moiety. The absence of any signal due to methyl ester ~50 ppm in **7** shows (Fig. 2) that the conversion to thioglycolic acid was complete. The ¹³C spectrum shows line broadening of all resonances relative to SiCH₂CH₂SCH₂CO₂H after introduction of palladium acetate (Figs. 2 and 3). If 1:1 palladium binding occurs then additional peaks due to PdOAc from fragments such as SiCH₂CH₂SCH₂CO₂PdOAc are expected in the solid state ¹³C NMR but its likely these are masked or very close to the thioglycolate resonances. Thus, the line broadening is consistent with the presence of Pd-free ligand and PdOAc complexed ligand.

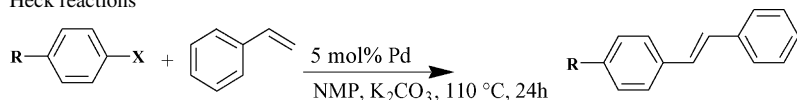
Material **8** was used as a heterogeneous catalyst for a range of Suzuki and Heck coupling reactions. The results are given above in Tables 1 and 2.

The choice of conditions used was based on those frequently reported for both homogeneous and heterogeneous catalysed Suzuki and Heck coupling reactions. Reports in the literature quote mol% catalyst used as a function of aryl halide in the range 0.01–5% [3,4,7]. In this work, 5 mol% catalyst was used. Under these conditions close to quantitative conversions were observed for the Suzuki reactions in less than 2 h. In an earlier trial Suzuki–Miyaura coupling reaction between bromoanisole and phenylboronic acid employing 2.5 mol% catalyst, 99% conversion was achieved but a longer reaction time ~7 h was

required. The longer time to achieve completion with 2.5 mol% may be an indication of substrate diffusion limitations in these sol–gel materials. Related studies using wider pore materials are underway. The Heck coupling was complete within 24 h and the catalysts could be recycled without loss in activity. In the case of the Suzuki–Miyaura reactions, the catalysts were recycled and slightly lower conversions (90%) were seen in the second and third cycles for some substrates after 1.5 h. The conversion was seen to increase in these cases at longer reaction times which is indicative of substrate transport limitations in the re-used catalyst. Leaching tests on hot filtrate to which fresh K₂CO₃ was added did not detect any palladium. This test included both assessment for further conversion in the hot filtrate and analysis for Pd in hot filtrates. If there is any equilibrium between solid and solution phase palladium during the reaction, the hot filtration and recycling data suggests this lies strongly in the direction of the solid-bound palladium. The activity is clearly preserved between runs. Assuming 1:1 binding, the analysis suggests approximately 15% of the thioglycolate sites in this supported Pd material are Pd free which should facilitate Pd rebinding in the event of solid solution equilibria.

Further work to explore the effects of varied Pd loading and a wider range of reaction conditions for this catalyst is in hand and the outcome of these studies will be reported in due course.

Table 2
Heck reactions



Aryl halide	%Conversion (cycle 1, cycle 2, cycle 3)
	99, 99, 98
	99, 99, 98
	98, 97, 97

Taken, 1.5 mmol styrene, 1.0 mmol aryl halide, 1.3 mmol K₂CO₃, 50 mg catalyst, 7 mL NMP. Conversion determined by GC all and NMR 4-bromoanisole and 4-bromotoluene.

3. Experimental section

3.1. General information

All reagents used were purchased from Aldrich, Avocado or Lancaster and were used without further purification, unless otherwise stated. Instruments: solution state ^1H NMR and ^{13}C NMR were recorded on a JEOL JNM-EX270 spectrometer (solvent CDCl_3 unless otherwise specified, lock and standard obtained automatically from the solvent used at 68 MHz); solid state NMR, Bruker AMX 600 MHz (^{29}Si SPE MAS, frequency 119.2 MHz, spinning speed 12 kHz; 1 min recycle delay, with $2\ \mu\text{s}$ – 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. Microanalysis were obtained from University College London Microanalysis Service and Medac Ltd. Analytical and Consultancy Services, London. Pd analysis was measured by AA or ICP-OES (sensitivity ~ 10 ppb).

3.2. Trimethoxysilylethylthio(methyl)glycolate **1**

A mixture containing trimethoxyvinylsilane (156 mL, 1.02 mol), methyl thioglycolate (87 mL, 0.97 mol) and di-*tert*-butyl peroxide (10 drops) was stirred at room temperature and then warmed to 115°C under an atmosphere of nitrogen. The mixture was maintained at this temperature for 1 h during which di-*tert*-butyl peroxide (10 drops) was added every 20 min. The solution was then cooled to room temperature to give methyl trimethoxysilylethylthio(methyl)glycolate. δ_{H} (CDCl_3): 0.76–0.81 (2H, bm, CH_2Si), 2.55 (2H, bm, CH_2S), 3.18 (2H, s, CH_2CO), 3.50 (9H, s, SiOCH_3), 3.66 (3H, s, OCH_3). δ_{C} (CDCl_3): 9.8 (SiCH_2), 26.7 (CH_2S), 32.9 (CH_2CO), 50.3 (SiOMe), 52.0 (OMe), 170.7 (CO).

The data for **1** are in agreement with those previously reported for the compound obtained from reaction of (chloroethyl)trimethoxysilane and sodium methoxycarbonylmethylthiolate [12].

3.3. Trimethylsilylethylthio(methyl)glycolate **2**

To trimethylvinylsilane (2.08 g, 20.72 mmol) was added methyl thioglycolate (2 g, 18.84 mmol) and few drops of di-*tert*-butylperoxide. The reaction mixture was stirred for 24 h at room temperature. The colorless mixture was purified by flash column chromatography using ethyl acetate:petrol (bp 40 – 60°C) (1:9) to obtain the methyl ester **2** as a colorless oil (2.77 g, 72%). δ_{H} (CDCl_3): 0.02 (9H, s, SiCH_3), 0.84 (2H, t, $J=4.2$, SiCH_2), 2.64 (2H, t, $J=4.9$, CH_2S), 3.21 (2H, s, $\text{CH}_2\text{CO}_2\text{Me}$), 3.71 (3H, s, OMe); δ_{C} (CDCl_3): 1.8 (SiCH_3), 16.7 (SiCH_2), 28.5 (CH_2S), 33.3 (CH_2CO), 52.3 (OMe), 171.1 (CO); m/z (ESI): 206 (M^+ , 5%), 146.1 (40%), 73.0 (100%). δ_{Si} (CDCl_3): 1.28.

3.4. Triphenylsilylethylthio(methyl)glycolate **3**

To triphenylvinylsilane (0.5 g, 1.75 mmol) was added methyl thioglycolate (0.16 mL, 1.75 mmol) and di-*tert*-butylperoxide was added every 2 h (3 drops) up to 6 h. The reaction mixture was heated at 70°C for 24 h. The colorless mixture was purified by flash column chromatography using ethyl acetate:petrol (bp 40 – 60°C) (1:9) to obtain a white solid **3** (0.51 g, 81%); mp: 60 – 62°C ; δ_{H} (CDCl_3): 1.76 (2H, t, $J=7.9$, SiCH_2), 2.80 (2H, t, $J=7.9$, CH_2S), 3.24 (2H, s, CH_2CO_2), 3.65 (3H, s, OMe), 7.23–7.60 (15H, m, *Ar-H*); δ_{C} NMR (CDCl_3): 13.9 (SiCH_2), 28.4 (CH_2S), 33.3 (CH_2CO), 52.4 (OMe), 171.1 (CO), 128.1, 129.8, 130.2, 134.1, 135.7 (*Ar-CH*), 170.9 (CO) δ_{Si} (CDCl_3): -11.60 .

Found: C, 70.55; H, 6.15; Calcd for $\text{C}_{23}\text{H}_{24}\text{O}_2\text{SiS}$: C, 70.37; H, 6.16.

3.5. Trimethylsilylethylthioglycolic acid **4**

To **2** (0.5 g, 2.43 mmol) was added 1 M sodium hydroxide (10 mL) and methanol (7 mL). The reaction mixture was heated at 50°C for 4 h. The aqueous layer was acidified to pH 2 by addition of 2 M HCl and the layers extracted with ethyl acetate. The organic layer was washed with brine and dried over MgSO_4 to give an yellow oil **4** (0.45 g, 96%). δ_{H} (CDCl_3): 0.06 (9H, s, SiCH_3), 0.80 (2H, t, $J=8.4$, SiCH_2), 1.28 (1H, bs, *OH*), 2.67 (2H, t, $J=8.4$, CH_2S), 3.19 (2H, s, $\text{CH}_2\text{CO}_2\text{H}$); δ_{C} (CDCl_3): 1.7 (SiCH_3), 16.7 (SiCH_2), 28.6 (CH_2S), 33.3 (CH_2CO), 177.3 (CO_2H); δ_{Si} (CDCl_3) 1.46. Calcd. for $\text{C}_7\text{H}_{16}\text{O}_2\text{SiS}$: C, 43.75; H, 8.33. Found: C, 43.50; H, 8.82.

Compound **4** was reported as product from trimethylvinylsilane and thioglycolic acid [13].

3.6. Triphenylsilylethylthioglycolic acid **5**

To **3** (0.5 g, 2.43 mmol) was added 1 M sodium hydroxide (10 mL) and methanol (7 mL). The reaction mixture was heated at 50°C for 4 h. The aqueous layer was acidified to pH 2 by addition of 2 M HCl and the layers extracted with ethyl acetate. The organic layer was washed with brine and dried over MgSO_4 to give a white solid **6** (0.45 g, 96%); mp: 64 – 66°C ; δ_{H} (CDCl_3): 1.77 (2H, t, $J=8.6$, SiCH_2), 2.85 (2H, t, $J=8.6$, CH_2S), 3.27 (2H, s, CH_2CO_2), 7.23–7.60 (15H, m, *Ar-H*); δ_{C} (CDCl_3): 13.9 (SiCH_2), 28.4 (CH_2S), 33.4 (CH_2CO), 128.0, 129.9, 130.2, 134.0, 135.1, 135.7 (*Ar-CH*), 176.5 (CO_2H); δ_{Si} (CDCl_3) -11.62 .

3.7. Ethylthioglycolic acid silica **7**

Compound **1** (25.4 g, 0.1 mol) and tetraethyl orthosilicate, TEOS, (223 mL, 1.0 mol) were dissolved in methanol (400 mL) and 1 M HCl (90 mL) was added with stirring. The mixture was then warmed at 80°C until the methanol had evaporated and a glass had formed. The glass was crushed and then stirred in refluxing methanol. The filtered material was then dried under reduced pressure of 0.1 mmHg at 80°C for 2 h to give the ethylthio(methyl)glycolate silica as a white powder **6**. A por-

tion of material **6** (3.14 g) suspended in 1 M hydrochloric acid (30 mL) was stirred at the reflux temperature for 2 h. The white solid was filtered, washed well with distilled water, methanol and finally with ether. The material was then dried under reduced pressure of 0.1 mmHg at 80 °C for 2 h to give the immobilised thioglycolic acid as a white powder **7** (2.9 g, 99%).

δ_C (CP MAS): 10 (SiCH₂), 25 (CH₂S), 33 (CH₂CO), 175 (CO₂H). δ_{Si} (MAS): -64 (T), -87, -98, -107 (Q); T:Q ratio 1:7 found equivalent to 1.6 mmol ethylthioglycolic acid per gram. Found *S* 1.3 mmol g⁻¹. Surface area 630 m²/g.

3.8. Palladium acetate ethylthioglycolate silica **8**

To a solution of **7** (1.0 g) in distilled water (15 mL) was added aqueous 1 M NaOH dropwise until pH 8.5 was achieved. The sodium thioglycolate salt formed was filtered off and washed with distilled water until the washings were neutral. The product was further washed with ethanol and ether. The white solid was dried under vacuum at 120 °C for 12 h to afford a white powder. A portion of this powder (0.5 g) was added to solution of palladium acetate (0.18 g, 0.81 mmol) in THF (50 mL). The mixture was stirred overnight and the orange solid formed filtered from the supernatant. The solid was washed well with THF and then dried under reduced pressure 60 °C at 0.01 bar to obtain **8**.

δ_C (CP MAS): 11 (SiCH₂), 22 (OAc/SCH₂), 36(CH₂CO), 181 (C=O).

3.8.1. Palladium analysis

A known weight of material was stirred in hot concentrated nitric acid for 6 h and the released palladium metal measured by atomic absorption gave 1.1 mmole Pd/g of material.

3.8.2. Leaching tests

A sample from the Suzuki reaction with bromoanisole was taken after 30 min 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 2.5 h. Conversion was found to be 17% at 30 min. Analysis showed no further conversion following this hot filtration. A sample of the filtrate was digested

and analysed for Pd. No Pd could be detected using a Spectro Genesis ICP-OES (sensitivity ~10 ppb).

The Heck reaction with bromoanisole was investigated for Pd leaching as described above with hot filtration after 8 h (50% conversion) and final assessment of conversion after 24 h. Once again analysis showed no further conversion following hot filtration and no Pd could be detected by ICP-OES analysis of this hot filtrate.

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