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Functionalized Mesoporous Silicates for the Removal of Ruthenium from Reaction Mixtures

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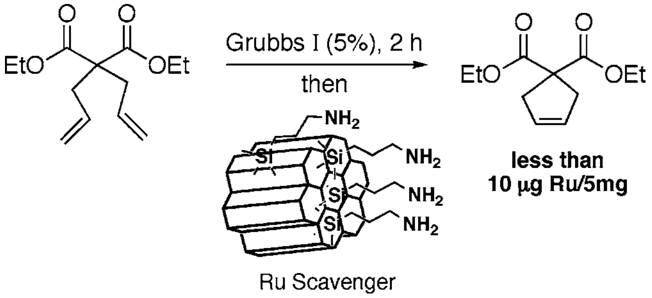
ABSTRACT



The removal of residual ruthenium after olefin metathesis reactions and asymmetric hydrogenations has been described using amine-functionalized mesoporous silicates. Aminopropyltriethoxy silane-derivatized silicates were found to be the most effective. More than 99.99% of $RuCl_3$ could be removed in a single treatment. Scavenging of Ru after metathesis reactions using a Grubbs generation 1 catalyst gave a product with concentrations of less than 10 μg/5 mg after two treatments with amine-modified silica. Most importantly, no chromatography was required.

Ruthenium catalysts are invaluable for affecting a variety of transformations, with the olefin metathesis reaction standing out as one of the most important reactions developed this past decade.[1] In addition, the direct hydrogenation and the transfer hydrogenation of olefins and ketones developed by Noyori and co-workers have revolutionized asymmetric synthesis.[2−5] Despite these facts, contamination of product mixtures with ruthenium has proven to be a significant problem. Colored ruthenium byproducts are reportedly present after the olefin metathesis and remain even after chromatography in some cases. In addition to the regulatory issues of metal contamination in the context of pharmaceutical synthesis, the presence of ruthenium after olefin metathesis reactions can cause isomerization of the installed olefin,[6] especially during distillation.[7] Finally, the removal of metal impurities from polymers prepared by either cross-coupling reactions[8] or metal-catalyzed living radical polymerizations[9] is of critical importance if the resulting materials are to be used in electronic applications.

Attempts to solve this problem can be divided into two classes, the preparation of supported ruthenium catalysts[10] and scavenging solutions after the use of homogeneous ruthenium. Although effective immobilized catalysts have been developed,[10−17] leaching can still be problematic. For

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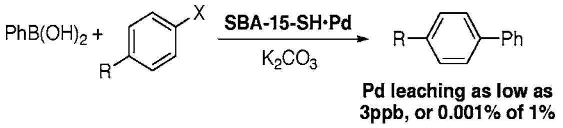
example, in the particular case of “boomerang” catalysts, a release and capture mechanism has been shown to be operative in some cases[18a] but not in others.[18b]

With respect to removing ruthenium after metathesis reactions, several interesting scavenging treatments have been attempted. These include treatment with simple resins,[19] treatment with phosphinated resins,[20] treatment with water-soluble phosphines,[7,21] addition of excesses of triphenylphosphine oxide followed by chromatography,[22] filtration through activated carbon followed by silica gel chromatography,[23] and addition of lead salts such as $Pb(OAc)_4$ followed by chromatography.[24] Although valuable, these methods do have drawbacks; most importantly, silica gel chromatography is required in most cases to bring the ruthenium content down to parts per thousand levels. Few methods actually bring the ruthenium contamination down to the parts per million level, with the best reported example being 60 ppm which is still above the level required for pharmaceutical applications (ca. 10−20 ppm).[25]

We and others have recently shown that chemically modified mesoporous silicates are highly effective scavengers for palladium.[26,27] Although both aminopropyl- and mercaptopropyl-functionalized silicates are effective scavengers, the thiols have the added advantage that after absorption of palladium highly active, leach-resistant catalysts result.[26,28] For example, treatment of mercaptopropyl-modifed mesoporous silica with $Pd(OAc)_2$ produces a material which catalyzes both Suzuki−Miyaura and Mizoroki−Heck reactions, with the leaching of palladium reaching levels as low as 3 ppb, corresponding to a loss of only 0.001% of the initially added catalyst (eq 1).[26] Furthermore, hot filtration tests, doping tests, and three-phase tests indicate that >95% of the reaction comes from a truly heterogeneous palladium species.[26]



(eq. 1)

Considering the demonstrated ability of porous silicates to remove ruthenium more efficiently than regular silica in chromatographic applications[29] and the use of natural zeolites to absorb ruthenium selectively from nuclear waste,[30] we embarked on a study of the ability of chemically modified mesoporous silicates to absorb ruthenium from metathesis and hydrogenation reaction mixtures.

We began the study of ruthenium scavenging by examining the removal of $RuCl_3{\cdot}3H_2O$ and bis(tricyclohexylphosphine) benzylidine ruthenium(II) chloride (Grubbs generation 1) from aqueous solutions (Table 1). A variety of functionalized silicates were examined. As expected, silicates functionalized with the more polarizable thiol **1**, which proved to be such an effective scavenger for palladium, were ineffective with the harder ruthenium(III) species. However, amine-functionalized silicates were found to be much more effective. Several ligands were compared including aminopropyltriethoxy silane (**2**), 3-(ethylenediamine) propyltrimethoxysilane (**3**), 3-(imidazol-1-yl) propyltriethoxysilane (**4**), and 3-(diethylenetriamino) propyltrimethoxysilane (**5**) (Figure 1). In addition, commercially available macroporous polystyrene scavengers (PL-EDA and PL-DETA, respectively) were also examined (Table 1). Scavenging studies were carried out at two concentrations of ca. 35 and 200 ppm. At low initial concentrations, the difference between the scavengers was marginal, but the most effective was SBA-15-**2** and SiO_2-**2** which removed 99.95% of the ruthenium from solution, bringing the initial 35−40 ppm solution to less than 30 ppb (average of five runs). All the

Table 1. Comparison of Amine Ligands on Different Supports for Scavenging of Ru at 35−40 ppm Initial Concentration[a]

		residual Ru in solution	
entry	scavenger	[Ru] (ppm)	% removed
1	SBA-15-**1**	31.5	25.5
2	SBA-15-**2**	0.017	99.94
3	SiO_2-**2**	0.027	99.94
4	SBA-15-**3**	0.139	99.64
5	SiO_2-**4**	0.05	99.86
6	SBA-15-**5**	0.277	99.28
7	SiO_2-**5**[b]	0.42	98.76
8	PL-EDA	0.13	99.66
9	PL-DETA	0.25	99.34

[a] Aqueous solutions of $RuCl_3{\cdot}3H_2O$ (10 mL) were treated with 100 mg of silicate for 1 h with stirring. See Supporting Information for full details. [b] $[Ru]_{initial}$ = 38.7 for most experiments, except entry 7, where it is 34.0 ppm.

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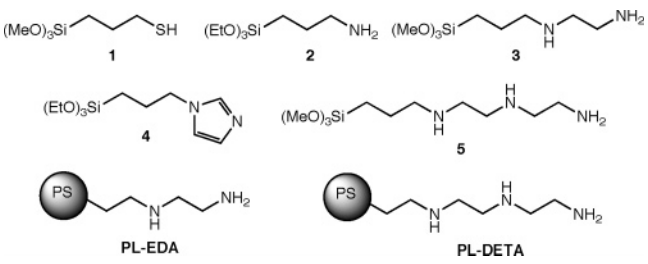


Figure 1. Ligands employed for the removal of ruthenium.

other amine-functionalized scavengers removed 98−99% of the ruthenium, whereas thiol-functionalized SBA-15 removed only 25% of the ruthenium.

At higher initial concentration, the difference between the scavengers became more apparent. SBA-15-**2** was the most effective scavenger, removing 99.99% of the ruthenium in the initial solution, which corresponds again to ruthenium levels of ca. 20 ppb remaining in solution (Table 2). The same amine scavenger on amorphous silica is not as effective, removing only 90% of the ruthenium.

Table 2. Comparison of Amine-Based Scavengers at High Initial Concentrations of Ru[a]

entry	scavenger	residual Ru in solution [Ru] (ppm)	residual Ru in solution % removed
1	SBA-15-**2**	0.02	99.99
2	SiO_2-**2**	21	90.0
3	SiO_2-**4**	57	73.0
4	SiO_2-**5**	2.2	98.9

[a] Aqueous solutions of $RuCl_3 \cdot 3H_2O$ (10 mL) were treated with 100 mg of silicate for 1 h with stirring. See experimental section for full details. $[Ru]_{initial}$ = 211 ppm.

Having established that SBA-15-**2** is the most effective scavenger for $RuCl_3 \cdot 3H_2O$, we then turned to the more pertinent test of removing the Grubbs catalyst (generation 1) using silicates modified with APTES (Table 3). Compared with similar initial concentrations of $RuCl_3 \cdot 3H_2O$, Grubbs catalyst is more difficult to remove; however, the scavenger is still very effective, and at initial concentrations of ca. 100 ppm or less, more than 96% of the ruthenium is removed, giving solutions that contain less than 10 ppm ruthenium. Again, the ordered silicate proved to be more effective at removing Ru at all concentrations tested.

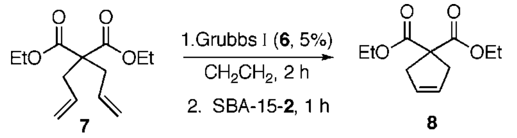
Finally, we examined the amine-modified silicate as scavengers for residual ruthenium remaining after a catalytic reaction. This is the most challeging test of the scavenger because the Ru may be present in a variety of different forms. Thus, we examined the removal of ruthenium after olefin metathesis reactions and hydrogenation of ketones. For the metathesis reaction, diallylmalonate (**7**) was treated with 5% of the Grubbs generation 1 catalyst (**6**) as shown in eq 2. Upon completion (2 h at room temperature), the reaction mixture was treated with either one or two portions of SBA-15-**2** for 1 h. The scavenging results are presented in Table 4.

Table 3. Removal of the Grubbs Catalyst (**6**) with SiO_2-**2** and SBA-15-**2** at Various Initial Concentrations[a]

entry	initial [Ru] (ppm)	residual Ru in solution [Ru] (ppm)	residual Ru in solution % removed
		SiO_2-**2**	
1	242	48.6	79.88
2	105	3.33	96.8
3	40.2	1.51	96.2
4	13.7	0.139	99.0
		SBA-15-**2**	
5	206	35.3	82.86
6	71.5	1.74	97.57
7	37.0	0.214	99.42
8	6.58	0.031	99.53

[a] THF solutions of the Grubbs catalyst (10 mL) were treated with 100 mg of silicate for 1 h with stirring.

Table 4. Removal of the Grubbs Catalyst (**6**) with SiO_2-**2** and SBA-15-**2** from Reaction Mixtures[a]



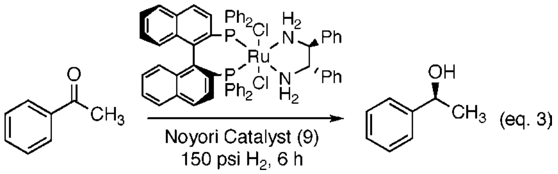
(eq. 2)

entry	initial [Ru] (ppm)[b]	residual [Ru] [Ru] (ppm)	residual [Ru] μg/5 mg	% removed
1	237 (126)	35.0	18.7	85.23
2	197 (105)	23.0	12.2	88.32
3	74.0 (34.9)	17.7	8.36	76.08
4[c]	66.8 (31.5)	18.3	8.64	72.60
5[d]	74.0 (34.9)	8.23	3.88	88.88
6[c,d]	66.8 (31.5)	11.6	5.49	82.63

[a] Grubbs metathesis reactions were treated with 100 mg of silicate for 1 h with stirring. [b] The number in parentheses is the concentration of ruthenium as μg/5 mg of product. [c] Scavenged with SiO_2-**2**. [d] The samples were treated with a second aliquot of silicate for 1 h.

Although the ruthenium concentrations in the product after scavenging with SBA-15-**2** or SiO_2-**2** are similar to those reported in the literature,[19,21,22] it should be noted that our method does not require chromatography as the final purification.[19,21,22]

Finally, we also examined the hydrogenation of acetophenone with Noyori's catalyst (**9**) as shown in eq 3. After hydrogenation at 150 psi for 6 h, the solution was treated with 250 mg of the modified silicate and filtered, and the resulting mixture was examined by ICPMS as described above.[31] Analysis by ICPMS indicated that only 0.17 ppm of ruthenium remained in solution, corresponding to the removal of 99.2% of the initial ruthenium catalyst added.



In conclusion, we have demonstrated that mesoporous silicates modified with aminopropyl triethoxysilane are effective scavengers for ruthenium, both in pure form as $RuCl_3 \cdot 3H_2O$ and bis(tricyclohexylphosphine) benzylidine ruthenium-(II) chloride (Grubbs generation 1) and after metathesis reactions and hydrogenations. Considering the ubiquitous nature of these reactions and the importance of removing ruthenium from the resulting product, this method promises to improve the applicability of ruthenium-catalyzed reactions.

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Supporting Information Available: Experimental procedures for the preparation of the supported reagents and for scavenging experiments and spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(31) The scale of the reaction was 2 mmol. For full details, see the Supporting Information.