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# The use of polyhedral oligomeric silsesquioxane (POSS) as a soluble support for organic synthesis: A case study with a POSS-bound isocyanate scavenger reagent

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ABSTRACT

The use of polyhedral oligomeric silsesquioxane (POSS) as a soluble support for use in organic synthesis is reported. A POSS-bound isocyanate was readily synthesised in one step from commercially available starting materials and isolated in high yield and purity by simple filtration. It was found to perform well as a scavenger for excess amine in the solution phase synthesis of amides and sulfonamides, allowing product isolation in high yield and purity.

The use of polymer-supported scavenger reagents is an area of great importance in organic synthesis, allowing the rapid removal of excess reagents from solution by a simple filtration without recourse to time-consuming purification protocols.[1] Such methodology, however, is not without its drawbacks and the use of insoluble polymer supports leads inevitably to heterogeneous reactions with slower reaction rates than their solution phase counterparts, to the need for large excesses of the reagent due to non-uniform accessibility of reactive sites and to the limitations on solvent choice due to polymer incompatibility. Various approaches have been attempted to overcome these limitations including the use of soluble polymeric supports[2] and chemical tagging with groups allowing extraction into specific solvents.[3] More recently the use of a tetraarylphosphonium salt as a solubility control group allowing the isolation of reagents by the addition of non-polar solvents was reported.[4]

Polyhedral oligomeric silsesquioxanes (POSS) feature a caged octacyclic inorganic silicon and oxygen framework surrounded on the exterior of the cage with eight organic substituents (Fig. 1).[5] POSS-containing materials have found use in a wide range of potential applications including medical devices,[6] OLEDS,[7] electronics[8] and packaging.[9] Additionally, POSS has been used as a support for metal catalysts,[10] allowing catalyst recovery through a nanofiltration process.[11]

During the course of our work using functionalised POSS materials we observed an interesting trend in solubility, that is, good solubility in many commonly used organic solvents such as dichloromethane, tetrahydrofuran, chloroform and petroleum ether. Conversely, in polar solvents such as acetonitrile, methanol, water and dimethyl sulfoxide the material was insoluble. Herein, we report our results in exploiting this differential solubility to use POSS as a soluble support for an isocyanate scavenger reagent. The POSS isocyanate **2** was synthesised in one step by the reaction between commercially available aminopropylisobutyl POSS, **1** and triphosgene (Scheme 1). This gave a near quantitative yield of **2** which was isolated as a free-flowing colourless solid by the evaporation of the reaction mixture and washing the residue with acetonitrile.[12] In addition to the use of **2** as a scavenger reagent, it may also be of interest to materials chemists working with POSS, as the isocyanate group offers a convenient handle for conjugation

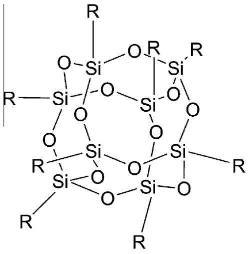

Figure 1.

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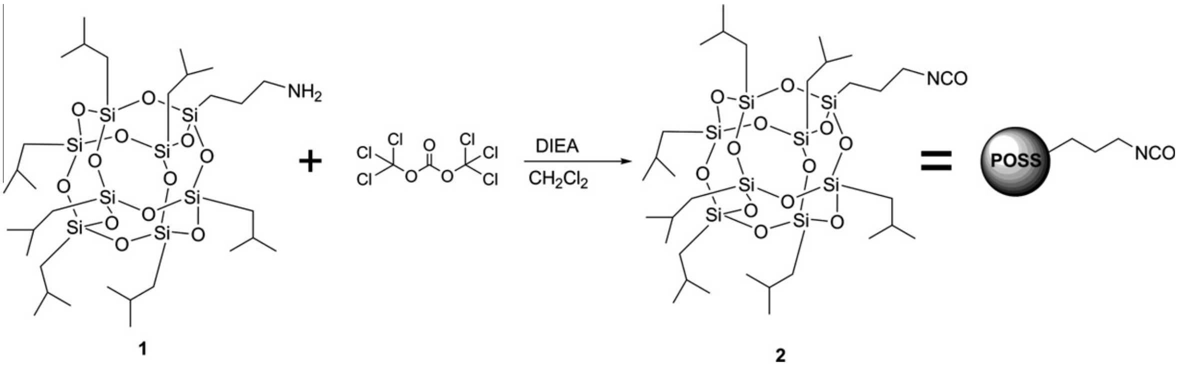


**Scheme 1.**

**Table 1**

| Entry | Amine scavenged (%)[a] | | |
|---|---|---|---|
| | Amine | POSS isocyanate **2** | PS isocyanate |
| 1 | *tert*-Butylamine | >95 | >95 |
| 2 | Benzylamine | >95 | >95 |
| 3 | Phenethylamine | >95 | >95 |
| 4 | Dipropylamine | >95 | >95 |
| 5 | Diisopropylamine | >95 | >95 |
| 6 | Diallylamine | >95 | 95 |
| 7 | Diallylamine[b] | >95 | 95 |
| 8 | Diallylamine[c] | >95 | 95 |
| 9 | Diallylamine[d] | >95 | 55 |
| 10 | Piperidine | >95 | >95 |
| 11 | 1,2,3,4-Tetrahydroisoquinoline | >95 | >95 |
| 12 | Morpholine | >95 | >95 |
| 13 | *N*-Methylaniline | 14 | 42 |
| 14 | *N*-Methylaniline[e] | 57 | 92 |
| 15 | *N*-Methylaniline[f] | >95 | >95 |

[a] Reaction performed with 0.214 mmol of isocyanate and 0.107 mmol of amine in $CDCl_3$ (1 mL) at 22 °C for 1 h. Extent of scavenging determined by $^1H$ NMR spectroscopy using $MeNO_2$ as an internal standard.

[b] Scavenger exposed to atmosphere for 14 days prior to reaction.

[c] Reaction performed in acetone-$d_6$.

[d] Reaction performed in petroleum ether.

[e] Reaction performed for 5 h.

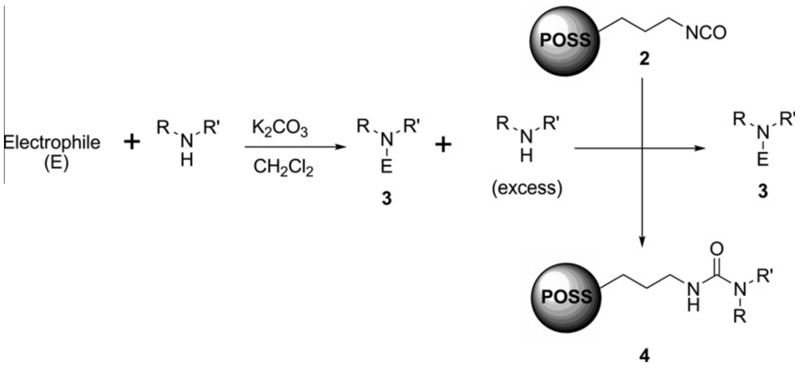
[f] Reaction performed for 18 h.

to nucleophilic groups. The synthesis of an octafunctional POSS isocyanate for the preparation of inorganic–organic hybrid materials via a hydrosilylation process has been reported previously.[13]

POSS isocyanate **2** gave a loading of 1.11 mmol of isocyanate per gram of material, a similar loading level to many commercially available polymer-bound reagents. It was envisaged that this loading could be further increased by the synthesis of POSS cores bearing more than one isocyanate moiety. Additionally **2** was found to be readily soluble in a number of organic solvents with a solubility of over 1 g per mL achievable in $CH_2Cl_2$. In order to determine the suitability of compound **2** for use as a scavenger reagent its ability to scavenge a variety of amines from solution was determined in comparison with a commercially available polystyrene-(PS)bound scavenger (Table 1).[14]

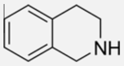
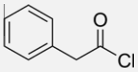
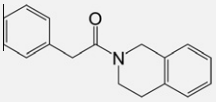
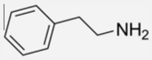
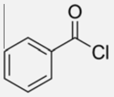
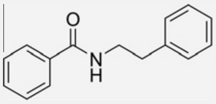
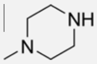
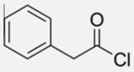
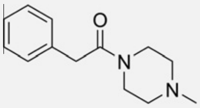
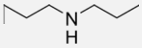
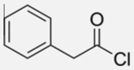
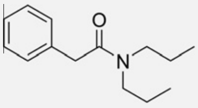
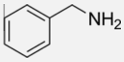
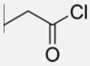
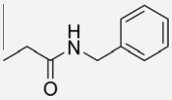
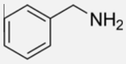
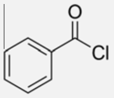
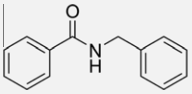
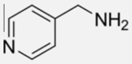
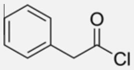
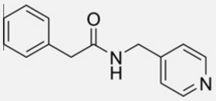
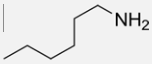
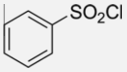
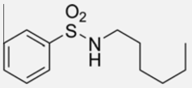
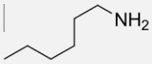
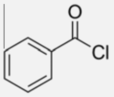
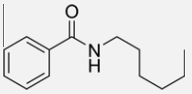
Compound **2** performed well with the complete scavenging of a variety of 1° and 2° amines (Table 1, entries 1–6 and 10–12). Unsurprisingly, the scavenging of *N*-methylaniline did not proceed to completion without extended reaction times (Table 1, entries 13–15). In common with the commercially available PS-bound scavenger, compound **2** was insensitive to atmospheric moisture with performance unchanged after 14 days of atmospheric exposure (Table 1, entry 7). Scavenging also proceeded in solvents where **2** was largely insoluble such as acetone (Table 1, entry 8), and in solvents where the commercial polymer-bound isocyanate reagent functioned poorly due to lack of polymer swelling, such as petroleum ether (Table 1, entry 9). In order to further evaluate the use of **2** it was used to scavenge excess 1° and 2° amines in the synthesis of a small array of amides and sulfonamides (Scheme 2) and the purity of the final products was evaluated (Table 2).

Formation of the products, **3** was achieved using 1 equivalent of electrophile and 1.5 equivalents of nucleophilic amine in the presence of an excess of $K_2CO_3$ as base. Subsequent scavenging of residual amine by **2** (1 equivalent) and its removal from the reaction mixture by precipitation with $CH_3CN$ and filtration gave the products in very good to excellent yields and with high purities (Table 2, entries 1a and 2–9). If desired, more than 90% of the mixture of unused **2** and quenched scavenger **4** could be recovered from the filter cake in high purity by extraction with $CH_2Cl_2$. This allows



**Scheme 2.**

**Table 2**

| Entry | Amine | Electrophile | Product | Yield[a] (%) | Purity[b] (%) |
|---|---|---|---|---|---|
| 1a |  |  |  | 90 | >95 |
| 1b[c] | | | | >95 | 70 |
| 2 |  |  |  | 91 | >95 |
| 3 |  |  |  | 88 | >95 |
| 4 |  |  |  | 92 | >95 |
| 5 |  |  |  | 92 | >95 |
| 6 |  |  |  | 91 | >95 |
| 7 |  |  |  | 90 | >95 |
| 8 |  |  |  | 98 | 94 |
| 9 |  |  |  | 85 | >95 |

[a] A mixture of amine (0.31 mmol) and $K_2CO_3$ (2.07 mmol) in $CH_2Cl_2$ (1 mL) was treated with electrophile (0.21 mmol) and stirred for 1 h. POSS isocyanate **2** (0.21 mmol) was then added and stirring continued for 1 h. The mixture was then reduced to low bulk under a stream of compressed air, diluted with $CH_3CN$ and filtered. The filtrate was evaporated in vacuo and extracted with $CH_3CN$, evaporation of which gave the desired products.

[b] Purity determined by GC and confirmed by $^1$H NMR spectroscopy.

[c] Reaction performed without scavenger.

the possibility of reuse and recycling of the scavenger reagent. When the reaction was performed in the absence of the scavenger a product of only 70% purity was obtained (Table 2, entry 1b).

In summary, in order to test the suitability of POSS as a soluble support for use in organic synthesis we have developed a POSS-bound isocyanate scavenger reagent, **2**. This material was isolated in one synthetic step in near quantitative yield, it exhibited similar reactivity to a commercially available polymer-bound scavenger and has been used to scavenge excess nucleophilic amine in the synthesis of an array of amides and sulfonamides. Removal of the scavenger by filtration resulted in the isolation of products in very good to excellent yields and with high purity.

## Acknowledgements

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## Supplementary data

Supplementary data (experimental procedures and data for all new compounds) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.07.015.

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12. *Experimental procedure*: A solution of aminopropylisobutyl POSS, **1** (10.0 g, 11.43 mmol) and *N*,*N*-diisopropylethylamine (3.98 mL, 22.87 mmol) in $CH_2Cl_2$ (150 mL) was treated portionwise with triphosgene (1.70 g, 5.72 mmol) and stirred at 22 °C for 2 h. The mixture was then evaporated in vacuo and the residue washed with $CH_3CN$ ($3 \times 100$ mL) and filtered. Drying at the funnel gave POSS isocyanate **2**, as a colourless, free-flowing solid (10.25 g, 100%). Mp 264–265 °C; $^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 3.28 (t, $J$ = 6.8 Hz, 2H), 1.96–1.70 (m,

9H), 0.96 (dd, $J = 0.8$ and 6.6 Hz, 42H), 0.71–0.51 (m, 16H); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 122.0, 45.2, 25.7, 25.1, 23.9, 22.5, 9.2; HRMS (EI) calcd for $C_{32}H_{69}NO_{13}Si_8$ [$M^+$]: 899.2918, found: 899.2895.

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