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A Highly Efficient and Recyclable Silica-Based Scandium(III) Interphase Catalyst for Cyanosilylation of Carbonyl Compounds

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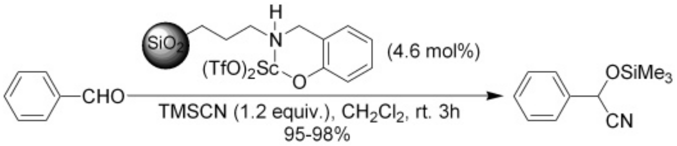
ABSTRACT



A new silica-based scandium(III) interphase catalyst 2 efficiently catalyzes the cyanosilylation of a variety of aldehydes and ketones. The catalyst shows high thermal stability (up to 300 °C) and also is stable in both organic and polar solvents. It also could be recovered and reused for at least 10 reaction cycles without considerable loss of reactivity.

Interest in scandium has increased recently due to the successful use of its compounds in organic chemistry.[1] Along this line, scandium triflate has been introduced as a promising mild, powerful, and selective Lewis acid for a variety of functional group transformations.[2] While most Lewis acids are decomposed or deactivated in the presence of water or protic solvents, Sc(OTf)$_3$, unlike other traditional Lewis acids, does not decompose or deactivate under aqueous workup conditions, and its recovery is often possible.[2,3] However, the most popular recycling methods for recovery of Sc(OTf)$_3$ are time-consuming and include the successive extraction of organic reaction mixture using deionized water.[2,3] Therefore, there is much room for the design and preparation of new versions of scandium-based catalysts to circumvent this problem without considerable loss of its catalytic power.

The heterogenization of inorganic reagents and catalysts useful in organic reactions is a very important area in so-called "Green" or sustainable chemistry.[4] One of the major goals is to facilitate easy separation of the final reaction mixture.[5] This feature can lead to improved processing steps, better process economics, and finally, environmentally friendly industrial manufacturing. However, traditional heterogeneous and supported catalysts are rather limited in the nature of their active sites and, thus, the scope and reproducibility of reactions that they can accomplish.[6] One way to overcome this uncertainty of the heterogeneous catalysts is to covalently incorporate an organic entity (flexible spacer) onto inorganic solids to create organic−inorganic hybrid (interphase) catalysts.[7] In these types of solid catalysts the

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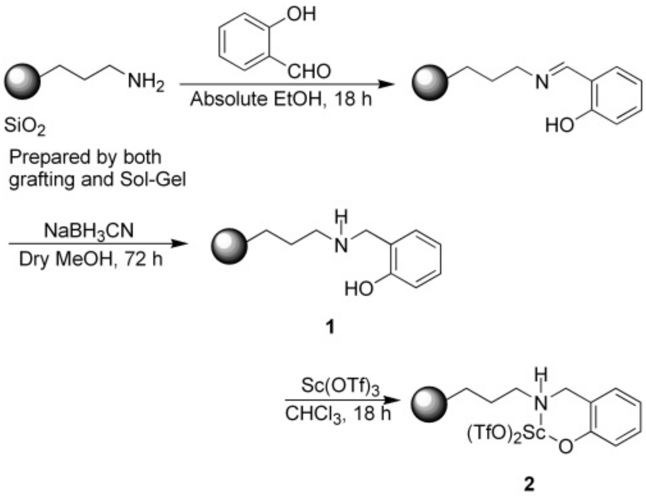
reactive center is highly mobile similar to homogeneous catalysts, and at the same time it has the advantage of recyclability. Recently, Kobayashi et al. have prepared a new polymer-supported scandium triflate which shows high activity in water.[8] While this is the first example of polymer-supported scandium, its preparation suffers from the drawbacks of the use of expensive starting organic polymers and reagents. However, to the best of our knowledge there are no examples of silica-based scandium(III) interphase catalysts. Herein we wish to present the design, synthesis, and catalytic properties of a novel Sc(OTf)$_3$-immobilized onto an organically modified silica (Scheme 1).[9] Our hypothesis was to change the expensive organic polymer chain to silica chain having spacers composed of a bidentate ligand to prepare a new immobilized silica-based scandium(III) interphase catalyst. Moreover, the presented bidentate ligand might be possible to replace by chiral analogues giving rise the corresponding chiral version of scandium for application in asymmetric transformations. Quantitative determination of the functional group contents of the surface-bound compound **1** was performed with thermogravimetric analysis (TGA). Typically, a loading at ca. 0.3 mmol•g^{-1} is obtained.

Scheme 1



Similarly, TGA/DTA analyses of immobilized scandium(II) were performed and showed a first peak due to the desorption of water (centered at 110 °C). This is followed by a second peak at 375 °C, corresponding to the loss of triflate groups accompanied by a third peak centered at 535 °C, which corresponds to the loss of the surface-bound bidentate ligand. Typical loading of scandium was determined using atomic spectroscopy (AA) and shows a loading 0.29 ± 0.01 mmol.g^{-1}. This result in combination with TGA analyses demonstrates that **2** corresponds to a 1:1 and 2:1 complex between surface bound and triflate ligands with scandium, respectively (Schemes 1 and 2).

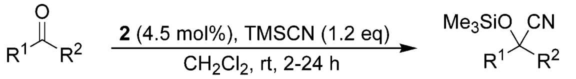
Table 1. Cyanosilylation of Carbonyl Compounds Using TMSCN in the Presence of Silica Based Scandium Interphase Catalyst **2**

entry	R^1	R^2	time (h)	yield^{a,b} (%)
1	Ph	H	3	95
2	Ph	H	24	0^c
3	Ph	H	3	45^d
4	3-(NO$_2$)C$_6$H$_4$	H	4	96
5	2-(NO$_2$)C$_6$H$_4$	H	4	98
6	4-(MeO)C$_6$H$_4$	H	4	95
7	4-(*i*-Pr)C$_6$H$_4$	H	2.5	97
8	4-(Cl)C$_6$H$_4$	H	3	92
9	3- Pyridyl	H	8	90
10	2,6-(Cl)$_2$C$_6$H$_3$	H	12	91
11	citral		4.5	90^e
12	PhCH=CH−	H	3	95
13	CH$_3$CH$_2$CH$_2$	H	5	94
14	CH$_3$(CH$_2$)$_5$	H	5	96
15	4-phenylcyclohexanone		5	94
16	cycloheptanone		6	92
17	cyclopentanone		6.5	95
18	CH$_3$(CH$_2$)$_3$	Et	12	70
19	PhCH$_2$	CH$_3$	12	80
20	4-(Ph)C$_6$H$_4$	CH$_3$	16	56^e

[a] Isolated yields. [b] The molar ratio of substrate/TMSCN/**2** is 1:1.2:0.0465. [c] The reaction was performed in the absence of **2**. [d] The reaction was carried out in the presence of the solid **2** for 1 h, and at that point the catalyst was filtered off and further stirring was done in the absence of catalyst for 2 h. [e] NMR yields.

In the course of preliminary studies of catalytic properties of **2**, we found that a small amount of 2 (0.15 g, ∼ 4.65 mol %) catalyzes efficient cyanosilylation of various types of carbonyl compounds (Table 1, Scheme 2).

Scheme 2



Cyanohydrin trimethylsilyl ethers are industrially valuable and important intermediates in the synthesis of cyanohydrins, β-amino alcohols, α-hydroxy acids, and other biologically active compounds.[10] They generally have been prepared by the reaction of a carbonyl with TMSCN in the presence of Lewis acids,[11] lanthanide salts,[12] base catalysts,[13] and solid base catalysts.[14] However, many of the existing methods for

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(9) For the details of experimental procedures and characterization of the catalyst, see the Supporting Information.

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this transformation have disadvantages such as prolonged reaction time,[13] the use of nonrecoverable catalysts,[10] and poor yields of the corresponding cyano trimethylsilyl ether especially in the case of ketones. Carbonyl compounds that were cyanosilylated in this way are benzaldehydes with both electron-withdrawing and electron-releasing groups including sterically hindered ones, aliphatic and α,β-unsaturated aldehydes, and cyclic, open-chain, and aromatic ketones. Representative results are shown in Table 1.

To show the catalyst's activity we have also performed cyanosilylation reaction of benzaldehyde using TMSCN in the absence of **2** under other similar reaction parameters. The reaction did not progress even after 24 h (Table 1, entry 2).

When using a supported catalyst two points become increasingly crucial issues. The first is the possibility that some active metal migrates from the solid to liquid phase and that this leached Sc^{3+} would become responsible for a significant extent of the catalytic activity. To rule out the contribution of homogeneous catalysis in the results shown in Table 1, the reaction was carried out in the presence of the solid **2** for 1 h, and at that point the catalyst was filtered off. The liquid filtrate was then allowed to react, but no significant conversion was observed after 3 h under the presented reaction conditions (Table 1, entry 3). This clearly indicates that no active species were present in the supernatant. Furthermore, the percent of scandium leaching was less than 1% of the surface-bound scandium even upon washing of the catalysts with deionized water. The second point is the deactivation and reusability of the **2**. It should be noticed that while most Lewis acids are decomposed or deactivated in the presence of protic solvents, the new heterogenized scandium catalyst is stable both in water and organic solvents and could be easily recovered and reused for at least 10 cycles without loss of yields of products. Recycling experiments were examined for the cyanosilylation of benzaldehyde. Thus, after the first run, which gave the corresponding cyanosilyl ether in 95% yield, after recovery the catalyst was subjected to a second cyanosilylation reaction from which it gave the cyanosilyl ether in 98% yield; the average chemical yield for 10 consecutive runs was 96%, which clearly demonstrates the practical recyclability of this catalyst (Figure 1).

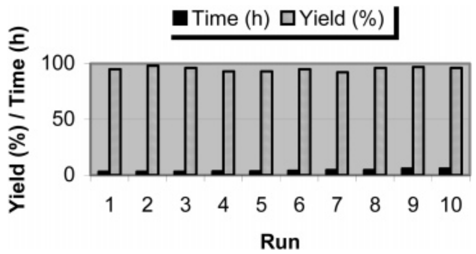

Figure 1. Recyclability of scandium catalyst **2** for the cyanosilylation of benzaldehydes using TMSCN.

As expected, owing to the steric bulk, the yields of the corresponding cyano trimethylsilyl ethers were moderate in the case of aromatic ketones (Table 1, entry 20). In contrast to aromatic ketones, however, the catalyst is quite effective for cyanosilylation of both cyclic and open-chain aliphatic ketones (Table 1, entries 15−19).

In conclusion, the novel silica-based scandium(III) interphase catalyst **2**, which can be prepared by simple operation from commercially available and relatively cheap starting materials, efficiently catalyzes the cyanosilylation of a variety of aldehydes and ketones. The catalyst shows high thermal stability (up to 300 °C) and also is stable in both organic and protic solvents. It also could be recovered and reused for several reaction cycles without considerable loss of reactivity. Owing to the bidentate model of the surface bound ligand in **2**, it might be possible to prepare chiral analogues of **2** using a chiral bidentate ligand. To our knowledge this is the first example of scandium-based interphase catalyst. The work on other applications of **2** and also preparation of its chiral analogues is currently ongoing in our laboratories.

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Supporting Information Available: Experimental procedures and ^{1}H and ^{13}C NMR spectra for new products and TGA for catalyst **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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