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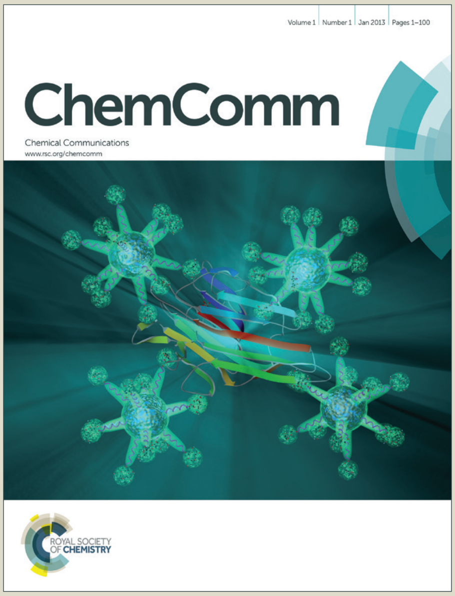

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Discovery of neat silica gel as catalyst: an example of S→O acetyl migration reaction[†]

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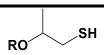
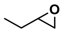
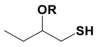
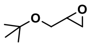
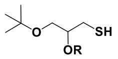
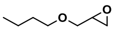
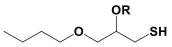
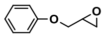
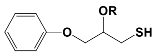
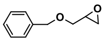
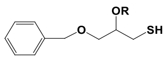
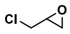
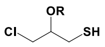
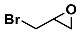
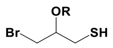
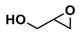
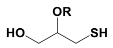
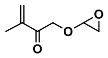
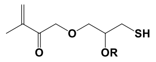
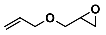
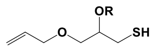
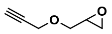
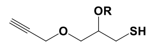
Silica gel, widely used in chromatography separation and as catalyst carrier, was employed here for the first time as fixed-bed catalyst for the S→O acetyl migration to synthesize thiol compounds under mild condition, showing merits of high efficiency, high selectivity, long-life recyclability, low cost and scalable availability.

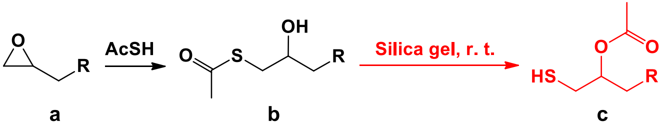
Silica gel plays an important role in modern chemistry as column packing materials for chromatography separation,[1] owing to its high selectivity and mechanical stability. Silica gel's another role in reactions is catalyst carrier, immobilized with organometallic compounds[2] or tethered with reactive functional groups.[3] However, little evidence for the catalytic activity of neat silica gel was found, only one example of silica gel catalysing the mesophilic anaerobic digestion of cow dung, but without any detailed explanations on this complicated process.[4] Given the characteristics of silica gel, like large specific surface area, porous structure,[5] low cost, scalable availability, it would trigger a potentially large change in catalyst application if silica gel showed high catalytic activity in wider fields.

Here we first report pristine silica gel itself, without any other combined compounds or modification, as an efficient fixed-bed catalyst with high catalytic activity under mild reaction conditions, catalysing S→O acetyl migration (Scheme 1) to obtain thiol compounds. We discovered that silica gel had high catalytic activity and selectivity, obtaining a series of thiol compounds with conversions over 90%, some even 100% in 9-14 hours without by-products. This high activity did not decline after being reused for more than 100 times, indicating rather long-life recyclability. The whole catalytic process is easily operated and environmentally friendly. The results suggest that some uncommon points may hide behind common things that we are seemingly familiar with, opening a new field of silica gel catalysis.

Table 1 Acetyl migration reaction of latent thiol compounds into thiol compounds catalyzed by silica gel fixed-bed.[A]

No.	Compounds (**a**)	Time /h	Products[B] (**c**)	Yield[C] /%	Conv.[D] /%
1		12		83	93
2		14		79	95
3		9		86	100
4		9		92	94
5		13		87	99
6		13		85	95
7		13		97	100
8		10		87	99
9		10		93	99
10		13		85	100
11		12		89	99
12		12		83	96

[A] Unless otherwise noted, all reactions were performed at room temperature. [B] Unless otherwise noted, the functional group of R stands for CH_3CO. [C] The purities of products were determined by ^1H NMR spectroscopy. [D] Conversion calculated by ^1H NMR spectroscopy.



Scheme 1 S→O acetyl migration reaction of latent sulphur compounds **b** into thiol compounds **c** catalysed by neat silica gel.

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‡ These two authors contributed equally.

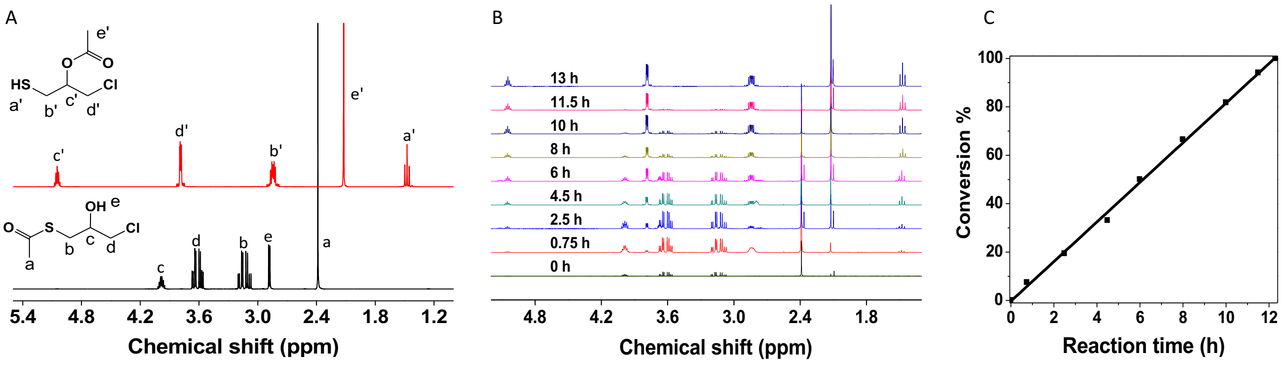


Figure 1 ^{1}H NMR (**A**) spectra in $CDCl_3$, its kinetics (**B**) and conversion (**C**) from **7b** to **7c**

Silica gel used in this work was commercially purchased. The catalytic potential of silica gel was demonstrated by S→O acetyl migration reaction using a variety of commercial epoxy compounds from **1a** to **12a**, shown in Table 1. First, the β-hydroxy thioacetates (**1b**-**12b**) were derived from the ring-opening reactions between epoxides and thioacetic acid (AcSH) in water with consistent stir at room temperature, and the conversion rates were almost 100% according to our analysis of ^{1}H NMR spectroscopy. Subsequently, the resulting latent sulfur compounds (**1b**-**12b**) were diluted with ethyl acetate, and slowly dropped into the silica gel fixed bed column (2 cm in diameter, 12 cm high) to be transformed into β-acetate thiols. Approximately 8.61 g silica gel is needed to produce 1 mmol thiol, but the silica gel used can be recycled. After standing still for 9-14 h, the oily products were eluted by around 190 ml a mixture of ethyl acetate and hexane (1:6), evaporated to obtain pure products as β-acetate thiols (**1c**-**12c**). The catalytic process in silica gel needed no stirring or heating, so it is green and energy-saving. Although a certain amount of solvent used in elution process can discount the greenness to some extent, fortunately the solvent be easily recycled through distilling and it is relatively nontoxic and innocuous.

The products (**1c**-**12c**) of 12 reactants above with different kinds of functional groups were determined by ^{1}H NMR, ^{13}C NMR (Figure S5-S28). They successfully transformed into corresponding thiol compounds, achieving high conversions ranging from 93% to 100% (**3a**, **7a** and **10a**) without by-products (e.g., intermolecular S→ acetyl migration) being detected, as summarized in Table 1. We als investigated the kinetics of the model reaction of **7b**→**7c** using silic gel as the catalyst. The conversion is linearly increasing upon the reaction time, and approaches 100% after 13 hours (Figure 1).

Notably, the results were almost the same using silica gel from different companies with different meshes (S1.1 and S8), demonstrating the generality of silica gel catalyst. All these resul s indicated broad functional group tolerance, short reaction time, hig selectivity and catalytic activity of silica gel catalyst.

To testify the real catalyst role of silica gel, we evaluated th recyclability of silica gel in the model reaction **7b**→**7c**. After bein used once, silica gel fixed-bed could easily be reused by simp

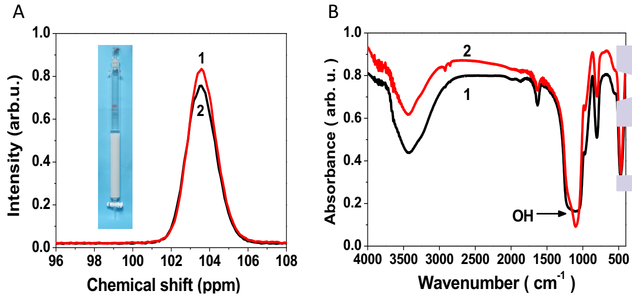


Figure 2 Comparison of the silica gel before (**1**) and after (**2**) being reused for 100 times by (**A**) XPS spectra, (**B**) IR spectra, indicating almost no chemical structure change.

Table 2 The reusability of silica gel in catalyzing the acetyl migration reaction from **7b** to **7c** [A].

Cycles	Conv [B]. /%	Yield [C] /%	Time /h
1	100	97	13
5	100	98	13
10	100	99	13
20	100	96	13
30	100	98	13
50	100	99	13
70	100	94	13
90	100	96	13
100	100	98	13

[A] Unless otherwise noted, all reactions were performed at room temperature with ethyl acetate as the solvent. [B] Conversion was calculated by ^{1}H NMR spectroscopy. [C] The purity was determined by NMR.

Table 3 Acetyl migration reaction of latent sulphur compounds **7b** into thiol compounds **7c** catalyzed by different catalysts.

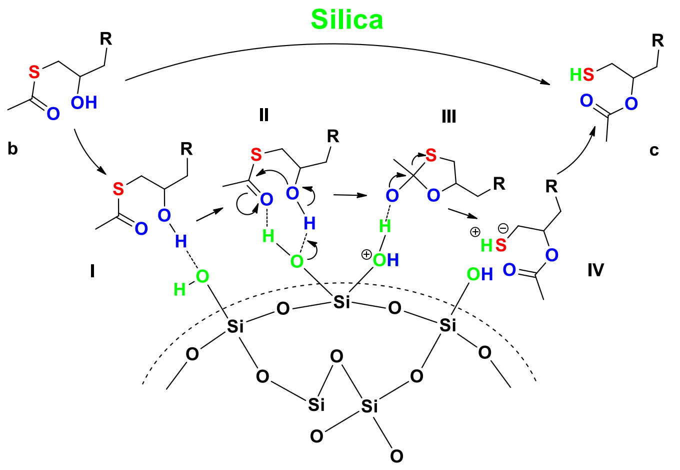
Catalyst	Reaction Condition	Conv. /%
Silica gel	r.t., 13h	100
Silicic acid	37°C, 1d	7
Acidic alumina	37°C, 1d	13
Aluminum oxide 150 basic	37°C, 1d	16
Silicon dioxide	37°C, 1wk	0

elution with ethyl acetate. Both yield (> 94%) and conversion (~100%) of product 7c kept constant at the same reaction time (13 h) after 100 cycles (Table 2). In case it decreases efficacy, it can be recovered by heating up to 300°C. This kind of catalyst is likely to be of profound commercial and economic significance in that they pave the way to the production of catalysts that facilitate the arrival of clean technology and green chemistry.

Silica gel catalyst provided a simple, facile and efficient method to the synthesis of thiol compounds. Many synthetic methods have been tried previously because thiol compounds are indispensable in organic chemistry including thiol-click reaction.[6] Sjoberg first reported gaining them through the S→O acetyl migration reaction catalysed by weak base (e.g., Na_2CO_3 and pyridine) and acids (e.g., AcOH).[7] However, results are not satisfactory because of the persistent challenges of multistep, relatively low yields, harsh conditions, and sulfide/disulfide by-products.[8] Until recent years, several catalytic systems were explored and higher yields were obtained. M. Abbasi reported a silica gel/triethylamine combined catalyst for acetyl migration reaction in 2012, and claimed that the presence of only silica gel or triethylamine would lead to rather low yields and serious side effects.[9] On the contrary, our group promoted the reaction conversions to over 86% with a sole triethylamine system,[10] and to near 100% with monolithic neat graphene oxide aerogel.[11] Clearly, silica gel used in this study was proved to be more efficient (>92%) and greener compared with triethylamine, more available and much cheaper compared with GO aerogel, showing industrial application potential.

The reason of why silica gel has this catalytic activity in catalyzing the acetyl migration reaction could be attributed to the silanol groups on its surface, and the reticular and porous structure. To infer the mechanism, we conducted control experiments with structural-similar solid acid including silicic acid, acidic alumina, aluminum oxide 150 basic and silicon dioxide, as listed in Table 3. Silicon dioxide did not have any catalytic activity because there are not any silanol groups on the surface. When catalysed by silicic acid, acidic alumina or aluminum oxide 150 basic, the yields are much lower than that catalysed by silica gel. It means that except for hydroxyl concentration, the synergistic effect in silica also enhances the catalytic activity. Additionally, the high collision frequency between the reagents and catalytic sites of silica gel in the confined space of the pores leads to high catalytic activity, similar to the case of GO aerogel.[11] The reason is that, the number of silanol groups per unit surface area is almost the same (4 and 5 OH groups nm^{-2}), among all kinds of silica,[5] and usually larger pore volume and smaller average pore diameter lead to larger BET surface area according to industrial information, which means more active sites (silanol groups) and higher catalytic activity.

Scheme 2 Proposed mechanisms of S→O acetyl migration reaction.



Based on the aforementioned experimental results and investigations of previous researchers,[12] we can conclude the active sites of silica gel catalyst are hydroxyl and proposed a reasonable mechanism of acetyl migration reaction (Scheme 2). At the beginning, β-hydroxy thioester (**b**) collides with the proton functional group of silica gel (**I**) via the formation of hydrogen bonds, making it possible to form a transitional hybrid silica-[illegible] membered ring (**II**). Then the labile large ring instantly disassociates into 5-membered ring intermediate,[13] plus Si-OH (**III**). Because sulfur is easier to be polarized than oxygen,[10] the ring opening occurs more often with the cleavage of S-C bonds than that of [illegible] bonds. Thus, the unstable 5-membered ring transforms into thiol product immediately (**IV**). Particularly, the beginning [illegible] determines the rate of the whole reaction.

It can be predicted that silica gel can be used as catalyst in other reactions. Silica gel belongs to solid acids which have been used as catalysts in various kinds of organic reactions for decades, due to their advantages of higher activity[12] and selectivity,[14] easier recycling and regeneration[15] compared with the liquid Brùnsted and Lewis acids.[16] Silica gel may surpass some other solid acids in catalytic properties as this work mentioned above.

In conclusion, we discovered neat silica gel as catalyst without loading extra catalytic compounds for the first time. The catalyst integrates advantages of high catalysis efficiency, high selectivity, high recyclability, cheapness and easy availability. It showed ultrahigh conversions (near 100%), high catalytic speed (9-14h) and wide application range at room temperature for the model reaction of S→O acetyl migration, in which silanol groups, synergistic effect and confined pore space in silica gel contributed to the catalytic activity. Silica gel is robust enough to be recycled 100 times without decreasing catalytic activity. All of these advantages suggest that silica gel, previously used as column packing materials for chromatography separation, is a potential catalyst for further study and practical use.

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