# ChemComm

## Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: S. P. Kitney, S. M. Sajedin, V. Rocher, F. Cheng and S. M. Kelly, *Chem. Commun.*, 2017, DOI: 10.1039/C7CC04952H.




ROYAL SOCIETY OF CHEMISTRY

rsc.li/chemcomm

View Article Online
DOI: 10.1039/C7CC04952H

ChemComm

COMMUNICATION

# Silicon diimide gel as an efficient stationary phase in thin layer chromatography for acid-sensitive organic compounds

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Stuart P. Kitney,[a] Seyed M. Sajedin,[a] Vincent Rocher,[a] Fei Cheng,[a] and Stephen M. Kelly[a]

**We report the use of mesoporous silicon diimide gel as a basic stationary phase in thin layer chromatography for the characterisation and purification of acid-sensitive compounds. The gel is prepared by a simple sol-gel process and exhibits a large specific surface area, almost monodisperse pores and basic properties due to free-hanging amine groups.**

Liquid-phase chromatography and purification over columns currently uses stationary phases based on two types of porous silica gel, $SiO_2$, either non-modified (normal phase) silica gel, such as DAVISIL®, or silica gel functionalised with long hydrocarbon chains (reverse phase).[1,2] Silica gel has a high surface area (usually around 600 $m^2$ $g^{-1}$) and is intrinsically acidic, which can lead to the degradation of acid-sensitive compounds, when using it as a stationary phase during column chromatography. A third, more recent method of silica gel functionalisation that successfully overcomes the acidic nature of silica is the reaction of amorphous silica with nonanoyl chloride to generate spherical silicon oxynitride (Sph-SiON).[3] However, this method reduces the pore volume and surface area of the porous silica precursor and has only been explored in high-performance liquid chromatography (HPLC).[4,5]

Organic compounds incorporating common protective groups, such as those with acetal, thioacetal, ether or silane functional groups, are especially labile and prone to decomposition on silica gel columns. Basic alumina (pH ~ 7-10) is an alternative to using silica gel. Unfortunately, it is hygroscopic, also decomposes a large range of organic compounds, often requires an aqueous pre-treatment to control compound specific activity and affinity and generally exhibits a low surface area, e.g., 200 $m^2$ $g^{-1}$.[6,7] Porous zirconia may allow the treatment of acid-sensitive compounds, but it also exhibits significant drawbacks in terms of cost, ease of use and reusability.[8]

Silicon diimide gel, $Si(NH)(NH_2)_2$, is an isoelectronic alternative to silica in chromatography. It is basic (pH ~ 7-10), mesoporous, e.g., pore size ~3.6 nm, exhibits a narrow pore size dispersity, possesses a large surface area, e.g., 600 $m^2$ $g^{-1}$, and its surface is covered with residual amine groups. The interactions with an analyte in chromatographic applications would involve surface nitrogen atoms and amine groups, strong electron donor interactions, as well as a good dispersive component, coming mostly from acid-base exchanges and hydrogen bonding. As such, it should be possible to control the retention times of analytes. Silicon diimide gel behaves like a soft base and should tolerate a wider range of functional organic groups than basic alumina and silica gel.

The surface energy of the silicon diimide gel used in this work was determined by the advancing and receding contact angles of different liquids through a drop under air according to the method of Van Oss *et al*.[9] It was determined as 52.6 mJ $m^{-2}$ with a strong electron donor contribution (46 $mJm^{-2}$) and smaller dispersive interactions (23.4 mJ $m^{-2}$). When compared to results from similar studies of silica and alumina surfaces,[10,11] silicon diimide gel features electron-donor interactions on a par with those of silica, but smaller than those of alumina, while the dispersive interactions are weaker than those of both, in spite of which the surface interactions of silicon diimide gel should be strong enough to retain analytes. This interaction with analytes is facilitated by the presence of NH and $NH_2$ groups, shown by the peak at 3400 $cm^{-1}$ in the FT-IR spectrum of the silicon diimide prepared in this work, figure 1. The strong band at 1000 $cm^{-1}$ is evidence for the n(SiN) vibration.

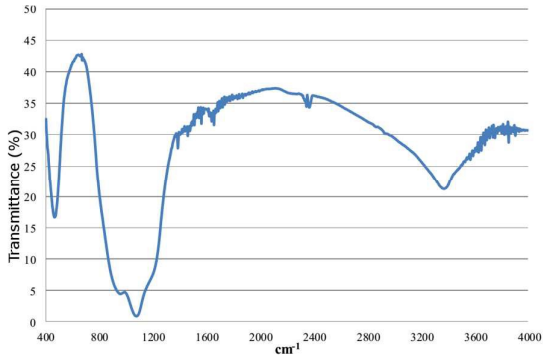



**Fig 1**. FT-IR Spectrum of Silicon Diimide gel.

[a] *School of Mathematics and Physical Sciences, University of Hull, Cottingham Road, Hull HU6 7RX, UK. Fax: +44 1482 466410; Tel: +44 1482 465219; E-mail: s.kitney@hull.ac.uk*

View Article Online
DOI: 10.1039/C7CC04952H




Silicon diimide gel can be prepared in a cost-effective, non-aqueous sol-gel process using *tris*(dimethylamino)aminosilane, $[(CH_3)_2N]_3SiNH_2$, prepared from *tris*(dimethylamino)silyl chloride, equation 1 and 2.[12,13] The mesoporous silicon diimide gel prepared in this way is stable in contact with water and air and can be regenerated after use by washing with a THF/$NH_3$ mixture. It has been studied as the inert support in membranes for the selective filtration of gas mixtures[14] at elevated temperatures, e.g., 400-600 °C, and in heterogeneous catalysts in various organic solvents and solvent mixtures including ethanol and water.[15,16] The present work reports proof of principle for the use of mesoporous silicon diimide gel as the stationary phase in thin film chromatography for acid-sensitive compounds.

$$3(Me_2N)_3SiNH_2 \xrightarrow[50\ ^oC]{CF_3SO_3H} [(Me_2N)_2SiNH]_3 + 3HNMe_2 \quad (1)$$

$$n[(Me_2N)_2SiNH]_3 + 6nNH_3 \xrightarrow{r.t.} 3[Si(NH)(NH_2)_2]_n + 6nHNMe_2 \quad (2)$$

**Equations (1) and (2)**. Two-step synthesis of silicon diimide gel.

The silicon diimide gel used in this work was prepared as previously reported.[11,12] It exhibits a large specific surface area (~700 $m^2\ g^{-1}$) and an almost monodiserse pore size (3.4 nm). These values compare well with those of standard silica (DAVISIL®), table 1, supplied by Sigma Aldrich, used as a reference solid phase in this study.

| | Surface Area ($m^2g^{-1}$) | Particle Size (μm) | pH (3 hours) | pH (12 hours) |
|---|---|---|---|---|
| silicon diimide | 700 | 10 – 40 | 7.4 | 9 |
| silica (Davisil) | 540 | 40 | 4 | 4 |

**Tab. 1** Properties of silicon diimide gel and silica gel (Davisil). pH determined by stirring 2-phneoxytetrahydropyran over the silica or silicon diimide in THF.

The silicon diimide gel has non-ideal particle size distribution, SEM images of silica gel, figure 2 (A), and silicon diimide, figure 2 (B), shows a variation of particle size from 10 – 40 μm, compared to a uniformly distributed 40 μm seen in silica gel. This is created during the processing of silicon diimide from the sol-gel solid. The diimide was broken up to form a powder using a simple, mechanical pestle and mortar process. Improving this process will give better particle size distribution. A simple automated ball milling process should prove to be a solution to this size distribution problem.

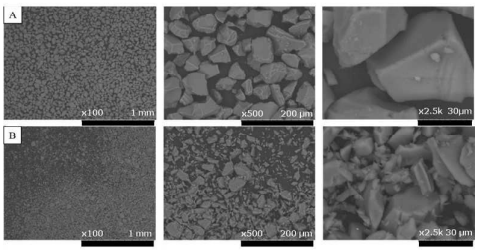
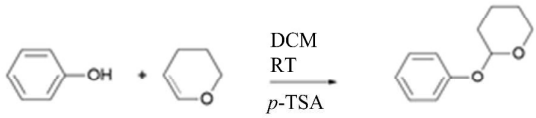



**Fig. 2** SEM images of commercial silica (A) and silicon diimide gel (B).

Synthesis of 2-phenoxytetrahydropyran was carried out, scheme 1, to yield an acid-labile test substance that was used to evaluate the suitability and efficiency of silicon diimide gel to act as an effective TLC stationary phase for this general class of acid-sensitive organic materials.




**Scheme 1** Synthesis of 2-phenoxytetrahydropyran

Silicon diimide gel was cast from ethanol as a slurry onto a glass microscope slide support to create a TLC plate. A binder was used, i.e., calcium sulphate (Gypsum 5% wt:wt), to fix the silicon diimide layer to the TLC plate and mechanically stabilise the stationary phase on the planar glass support in the presence of a variety of solvents commonly used in thin layer chromatography. In the interests of simplicity, a fluorescent material was not added to the stationary phase, instead an iodine developing tank was used to expose analyte movement up the plate, allowing calculation of retention factors (Rf) and visibility of analyte movement, figure 3.

Figure 3 shows the use of mesoporous silicon diimide gel as a stationary phase for TLC applications using 2-phenoxytetrahydropyran as a typical acid-sensitive test compound incorporating a common protecting group for alcohols. Two TLC plates, one incorporating glass-supported silicon diimide, top plate figure 3, as the stationary phase and the second aluminium-supported plate covered with a standard silica gel stationary phase are shown in Figure 3. Both plates in figure 3 were prepared with three spots, A, B and C. A is a spot of reaction starting material, phenol. Spot B was a co-spot of the reaction mixture and starting material A. Spot C was the reaction mixture on its own. Dihydropyran was not used as a spot on the TLC plate, because of its high volatility it tends to spread the solutes. A mixture of hexane:dichloromethane (95:5) was used as the mobile phase. There is a clear chromatographic effect with both stationary phases. The highest retention factor (Rf) was observed for the expected product 2-phenoxytetrahydropyran, 0.34 and 0.36 were recorded for silicon diimide and silica gel respectively.

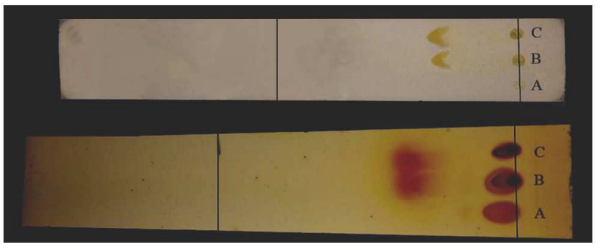
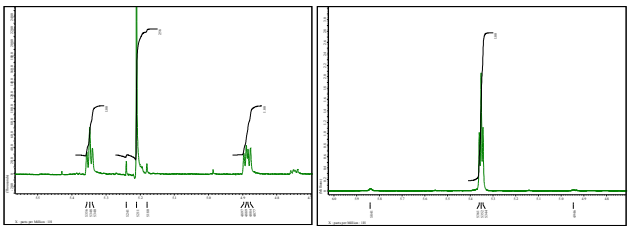



**Fig. 3** TLC analysis of the reaction mixture, shown in scheme 1, on a silicon diimide plate (top) and a silica gel plate (bottom), run using a (95:5) mixture of hexane:dichloromethane as eluent. A is a spot of the phenol starting material. Spot B is a combined spot of the reaction mixture and the phenol starting material. Spot C is the reaction mixture shown in scheme 1.

View Article Online
DOI: 10.1039/C7CC04952H




It is impossible to determine - due to the non-quantitative nature of TLC analysis - whether the intense spot C at the origin of the silica gel TLC plate (bottom) is representative of unreacted phenol in the reaction mixture or is due to 2-phenoxytetrahydropyran being decomposed on the silica gel stationary phase. TLC is also a rapid process compared to column chromatography, which can take many hours. This makes acid-labile compounds more susceptible to decomposition during column chromatography. To determine the unstable nature of 2-phenoxytetrahydropyran over silica gel and silicon dimimide a second experiment was designed. Identical solutions (1 mol $L^{-1}$) of 2-phenoxytetrahydropyran in tetrahydrofuran were stirred over of either mesoporous silicon diimide gel or silica gel at room temperature and the pH monitored after 3 hours and 12 hours, table 1. The solution in contact with silica gel became acidic (pH = 4) quickly, i.e., less than 3 hours. The test mixture containing silicon diimide gel gradually became basic (pH = 9), over 12 hours, due to the presence of silicon diimide gel. This pH change in the presence of silica is expected to be large enough to decompose acid-labile materials.



**A** **B**

**Fig.** 4. NMR Spectra of 2-phenoxytetrahydropyran after 3 hours stirring over silica, **A**, and 2-phenoxytetrahydropyran after 3 hours stirring over silicon diimide, **B**.

The THF solvent was removed from the 3 hour samples and the NMR recorded using $CDCl_3$ as solvent and TMS as internal standard, figure 4. NMR **A** shows that the $H_\beta$ triplet (5.34 ppm) was gradually replaced over 3 hours by a composite peak comprised of the $H_\alpha$ broad phenolic singlet (5.21 ppm) and the $H_\gamma$ hemiacetal triplet, (4.89), in the presence of silica gel. The number of protons represented by this composite peak also increased relative to the number of protons of the phenyl ring, in agreement with the replacement of one $H_\beta$ by one $H_\alpha$ plus one $H_\gamma$. The formation of the $H_\gamma$ hemiacetal triplet and $H_\alpha$ broad phenolic singlet was not observed in NMR **B**. This is evidence that gradual decomposition of 2-phenoxytetrahydropyran occurs in the presence of silica gel. While TLC may be a too rapid process to see significant degradation of 2-phenoxytetrahydropyran, it is clear that silicon diimide would be the preferred stationary phase to protect against acid-labile decomposition.

THP is a typical protecting group used for alcohols and phenols in organic synthesis. 2-phenoxytetrahydropyran utilises the THP protecting group and we have shown that it is hydrolysed to form phenol and tetrahydropyran by the acidic nature of the silica gel. No such changes were observed in the solution in contact with the silicon diimide gel under identical conditions. The triplet at 5.35 ppm was still observed with the same relative intensity after 24 hours of stirring in the presence of silicon diimide.

An up-scaled process for the reproducible fabrication of uniform TLC plates in standard plate sizes, also incorporating a fluorescent compound, such as manganese-activated zinc silicate, for use in combination with standard UV-lamps, remains to be developed. Similarly, processes for the fabrication of ranges of granule size of mesoporous silicon diimide gel for use as the stationary phase in chromatography columns will also need to be developed. This would allow this new, highly stable and basic chromatographic stationary phase to have considerable potential use in GLC, GPC and HPLC applications.

In summary, we have shown that mesoporous silicon diimide gel $Si(NH)(NH_2)_2$ is a suitable, efficient, and stable stationary phase for thin layer chromatography. It has been shown using a model system that mesoporous silicon diimide gel has the capacity to separate organic compounds chromatographically without decomposing acid-sensitive functions or bonds. It provides an alternative to either basic alumina, base-doped silica gel or silicon oxynitride for use as a chromatographic stationary phase in the identification and purification of acid-labile organic compounds, such as pharmaceutical intermediates or final products.

**Notes and references**


1. L. F. Giraldo, B. L. Lopez, et al., Macromol. Symp., 2007, **258**, 129-141.
2. I. M. El-Nahhal and N. M. El-Ashgar, J. Organomet. Chem., 2007, **692**, 2861-2886.
3. H. Wan, X. Xue, Y. Du and X. Liang, Anal. Methods, 2012, **4**, 3524.
4. H. Wan, Q. Sheng, H. Zhong, X. Guo, Q. Fu, Y. Liu, X. Xue and X. Liang, J. Sep. Soc. 2015, **38**, 1271.
5. H. Wan, H. Zhong, X. Xue, X. Liang, J. Sep. Sci. 2016, **39**, 3860.
6. J. J. Kirkland, J. Chromatographic Sci., 1996, **34**, 309-313.
7. Y. Mao and B. M., J. Chromatography A, 1997, **790**, 9-15.
8. M. Grun, A. A. Kurganov, et al., J. Chromatography A, 1996, **740**, 1 -9.
9. C. J. Vanoss, R. F. Giese, et al., J. Adhesion Sci. Technol., 1992, **6**, 413-428.
10. E. Chibowski, Abstracts Amer. Chem. Soc., 1992, **203**: 262-COLL.
11. W. Wu, R. F. Giese, et al., 1996, **89**, 129-132.
12. R. Rovai, C. W. Lehmann, et al., Angew. Chem. Int. Ed. Eng., 1999, **38**, 2036-2038.
13. F. Cheng, S. Clark, et al., J. Amer. Cer. Soc., 2004, **87**,1413-1417.
14. F. Cheng, S. M. Kelly, et al., J. Membrane Sci., 2006, **280**, 530-535.
15. F. Cheng, S. M. Kelly, et al., Chem. Mater., 2006, **18**, 5996-6005.
16. S. P. Kitney, F. Cheng, S. Khan, C. N. Hope, W. McNab and S. M. Kelly, Liq. Cryst., 2010, **38**(8): 1027 - 1033.