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Silica-bonded calixarenes in chromatography

I. Synthesis and characterization by solid-state NMR spectroscopy

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Abstract

Two different reaction schemes have been used to synthesize silica-bonded calixarene phases. Specifically, a triethoxysilyl calix[4]arene is reacted with silica to produce a bonded calix[4]arene tetraamide phase, and a hydride-derivatized silica undergoes a hydrosilylation reaction with *p*-allylcalix[6]arene hexaester to give a calix[6]arene hexaester phase. The resulting products were characterized by ¹³C and ²⁹Si cross polarization/magic angle spinning NMR spectroscopy. The spectra clearly show calixarene bonding to the silica surface and are invaluable in determining the nature and extent of chemical modification of the surface with these macrocyclic compounds.

Keywords: Nuclear magnetic resonance spectrometry ; stationary phases, LC; Calixarenes

1. Introduction

The chemical immobilisation of selective macrocyclic compounds to the surface of silica can lead to materials with important applications in separation and sensor science. The chromatographic selectivity for amino acid esters and for alkali metal ions on silica bonded calix[4]arene tetraester stationary phases has recently been described [1]. In addition, octadecyl silica and XAD resin can be rendered chelating for metal ions by the immobilisation of

macrocyclic ligands such as calix[4]arene tetrahydroxamate [2]. Whatever the application, it is clear that detailed information on the surface bonded chemistry such as can be provided by solid-state NMR, is crucial to understanding the functional aspects of the phase. To date, little work has been reported on the characterization of silica bonded calixarene phases.

The chemistry of attachment of the calixarenes to silica can be carried out using standard organosilane reaction or by use of hydride silica, which is reported to provide greater hydrolytic stability [3,4]. In this paper, the utility of ²⁹Si and ¹³C solid-state NMR spectroscopy in the characterization of new silica-bonded calixarene phases is demonstrated.

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2. Experimental

2.1. Silica-bonded calixarenes

Two silica-bonded calixarene phases A and B were prepared using two distinct chemical routes. Silica-bonded calixarene phase A was prepared by refluxing ca. 0.32 g of the triethoxysilyl derivative of the calix[4]arene tetraamide (Fig. 1, I) in 30 ml toluene with 2.0 g of activated Nucleosil (5 μm , Machery and Nagel, Germany) for 24 h. Following filtration, the silica phase was washed with ca. 100 ml toluene and yielded 6.7% C on elemental analysis. This approach has been used previously by the authors to produce silica-bonded calix[4]arene tetraester stationary phases [1].

Silica-bonded calixarene phase B was prepared using an alternative method detailed here based on hydride silica. Into a three-necked round bottom flask with stirrer, inner thermometer and a Y-piece with reflux condenser and a pressure equalized dropping funnel with teflon stopcock (without any use of grease for tightening), was placed 4.8 g LiChrosorb SI 100, particle diameter 10 μm (Merck, Germany), 100 ml of freshly distilled dioxane and 7 ml 2.3 M aqueous HCl. At 70–80°C and with slow stirring, 2.6 g (3.0 ml) dimethoxy methylsilane $(\text{CH}_3\text{O})_2\text{CH}_2\text{SiH}$ (density 0.861) (IR: 2180 and 2162 cm^{-1}) in 50 ml dioxane was added dropwise

within 30 min. After refluxing for 1.5 h and standing overnight, the slurry was filtered and the modified silica gel was washed with tetrahydrofuran, tetrahydrofuran– H_2O (80:20, v/v), tetrahydrofuran, and diethyl ether (50 ml each in portions of 10 ml). After drying at room temperature, one band at 2180 cm^{-1} in nujol suspension was observed [$(\text{CH}_3\text{O})_2\text{CH}_2\text{SiH}$ gave bands at 2180 and 2162 cm^{-1}]. Elemental analysis yielded 1.75% C and 1.18% H.

p-Allylcalix[6]arene hexaester (0.38 g) was dissolved in 45 ml toluene (some black oil was removed from this solution). To this solution, 120 μl of 0.1 M H_2PtCl_6 (ca. 10^{-5} mol) in isopropanol was added and the mixture was boiled at reflux for 1.5 h. After cooling and separating again some black oil from the yellow–orange solution, 2.2 g of the above modified SiH-silica gel was added. The slurry was boiled under reflux and streaming N_2 for 16 h. After addition of a further 3 mg H_2PtCl_6 in 0.2 ml isopropanol and boiling under reflux for 6 h (colour yellow–brown), the slurry was filtered and washed in the same way as the hydride silica above and dried under vacuum at 80°C for 6 h. Elemental analysis yielded C 5.95% and H 2.0%.

2.2. CP/MAS NMR spectroscopy

Details of the solid-state NMR spectroscopy are as follows: CP-MAS (cross polarization/magic angle spinning) NMR measurements were performed on a Bruker ASX 300 spectrometer on samples of the various calixarene-bonded stationary phases. All spectra were recorded using a CP pulse sequence with phase cycling. For ^{29}Si CP/MAS NMR measurements the samples (200–300 mg) were packed in 7 mm double bearing rotors of zirconium oxide. Magic angle spinning was carried out at a rate of 4000 Hz. The pulse length amounted to 6.5 μs and the contact time was 5 ms. For each spectrum typically 10 000 scans were accumulated with a repetition rate of 1 s. ^{13}C CP/MAS NMR measurements were performed with samples (100 mg) packed in 4-mm double bearing rotors of zirconium oxide which allowed to carry out magic angle spinning at a rate of 10 000 Hz. A pulse length of 4 μs was used, the contact time was 3 ms and the

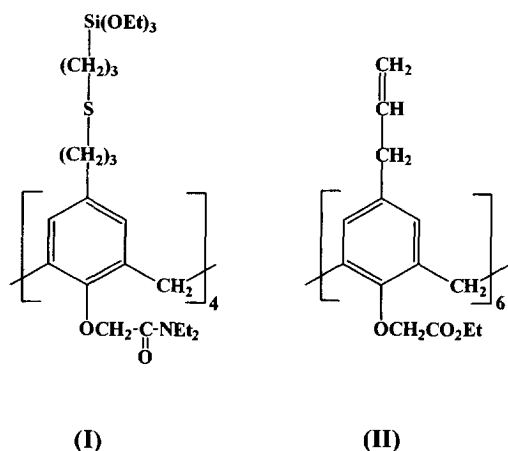


Fig. 1. Calixarene derivatives used to prepare bonded-silica phases A and B (see text) respectively. (I) Triethoxysilyl derivative of a calix[4]arene tetraamide. (II) *p*-Allylcalix[6]arene hexaester.

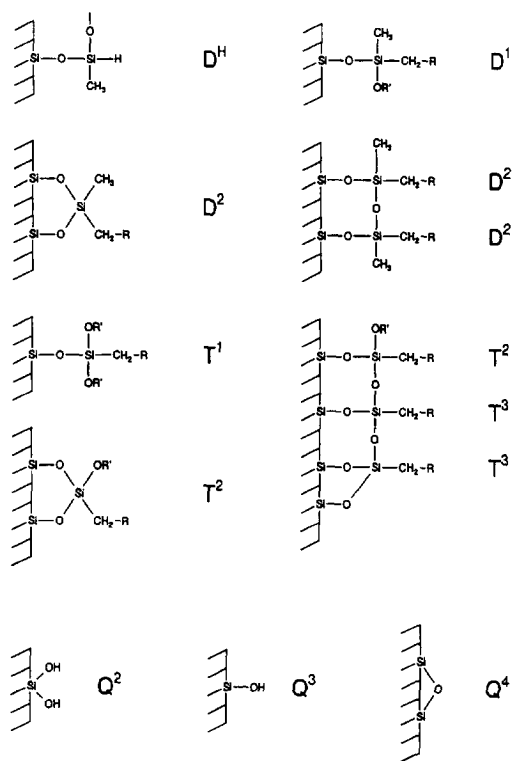


Fig. 2. The various types of silicon groups likely to be found on the surface of calixarene-bonded silicas. The lettering is used in the subsequent CP/MAS NMR spectra.

repetition rate was 2s. For the ^{13}C solid-state NMR spectra 80 000 scans were accumulated. All NMR spectra were externally referenced to liquid tetramethylsilane.

3. Results and discussion

3.1. ^{29}Si CP/MAS NMR spectroscopy

Previously we have successfully used solid-state NMR to characterize bonded phases for HPLC [5–8] and the resonances for the various groups present on the surface of the silica have been assigned (see Fig. 2). The ^{29}Si CP/MAS NMR spectra for the bonded calixarene silica phases A and B are shown in Fig. 3 and Fig. 4. The spectrum of silica bonded calixarene phase A in Fig. 3 shows two groups of peaks. In the region from -90 to -110 ppm appear the resonances of the surface silicon atoms present on the silica gel [8]. The resolution is sufficient to distinguish between the silanediols [-90 ppm, $\text{Si}(\text{OH})_2$, Q^2], silanols (-100 ppm, SiOH , Q^3) and siloxanes (-110 ppm, SiOSi , Q^4). The second group of peaks in this spectrum, covering the range -47 to -60 ppm indicate that the silica gel has been

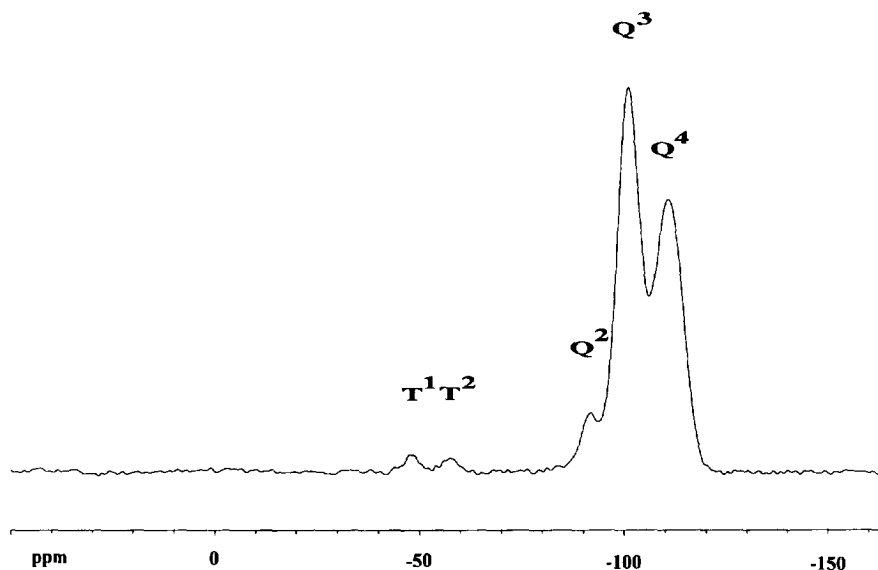


Fig. 3. ^{29}Si CP/MAS NMR spectrum of silica-bonded calixarene phase A. See Fig. 2 for key to signal assignments.

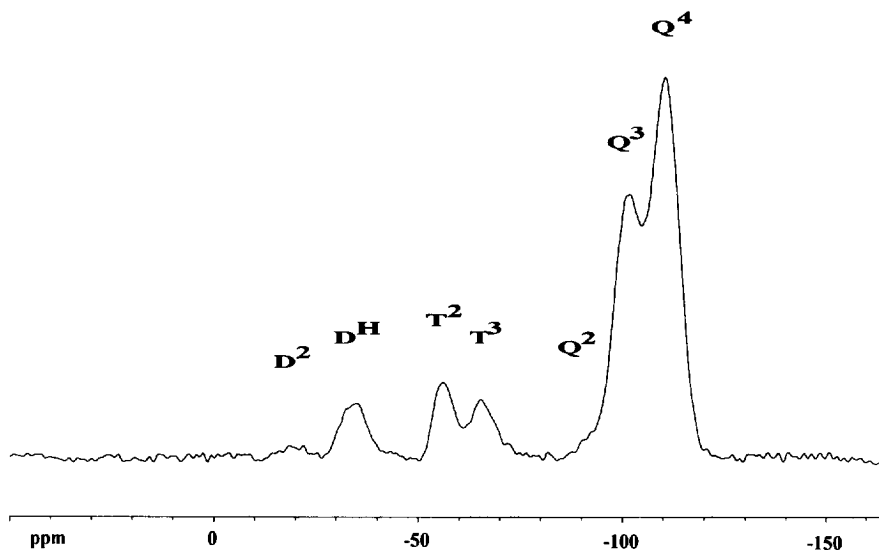


Fig. 4. ^{29}Si CP/MAS NMR spectrum of silica-bonded calixarene phase B.

modified by reaction with a trifunctional alkylsilyl group. The exact chemical shift of the signal is dependent on the degree of crosslinking. Thus monodentate bonded and non-crosslinked silicons appear at -47 ppm (T^1) while bidentate bonded silicons appear at -57 ppm (T^2). The intensities of the T-group peaks are relatively small whereas the silanol and silandiole peaks appear very intensive. Both facts indicate that only a small amount of the trifunctional silane has been bonded to the silica surface and a high degree of surface Si-OH groups are still present. About 50% of the silanes are bonded only over one Si-O-Si- bridge to the surface. The remaining trifunctional silanes are bonded bidental to the silica gel surface. A crosslinking between the bonded silanes seems not to be very probably because of the spatial distance between such groups. The ^{29}Si CP/MAS NMR spectrum of silica bonded calixarene phase B looks quite different (Fig. 4). Besides the Q- and T-groups further peaks are identifiable in the range between -15 to -40 ppm according to the signals of difunctional alkylsilanes bonded to the surface. The highfield peak at -35 ppm (D^{H}) is due to bonded methyltrimethoxysilane while the D^2 -peak at -18 ppm indicates those surface-bonded silanes which have undergone the hydrosilylation addition reaction.

The intensity pattern of the peaks shows some interesting aspects. A nearly disappeared Q^2 peak additionally to a relative weak Q^3 peak indicates that most of the surface Si-OH groups have been chemical modified. However most of the dimethoxymethylsilanes bonded to the surface in the first reaction step have been hydrolyzed and crosslinked seen by the very intensive signals at -56 ppm and -65 ppm (T^2 - and T^3 -groups respectively). A significant amount of methylsilanes has not reacted further. Only the very small portion of the silanes were active in the hydrosilylation reaction which is indicated by the presence of the D^2 -groups.

3.2. CP/MAS NMR spectroscopy

The ^{13}C CP/MAS NMR spectrum of silica bonded calixarene phase A shows clearly that the calixarene is really bonded to the silica gel surface. Peak assignment is made in Fig. 5a. The resolution of the spectrum is good enough to distinguish between the carbon atoms of the calixarene, the spacer to the silica surface and the atoms of the side chain. The high intensity of the peaks in the aromatic region additionally to the peak of C-7 indicate that a relative high amount of the calixarene is chemically bonded

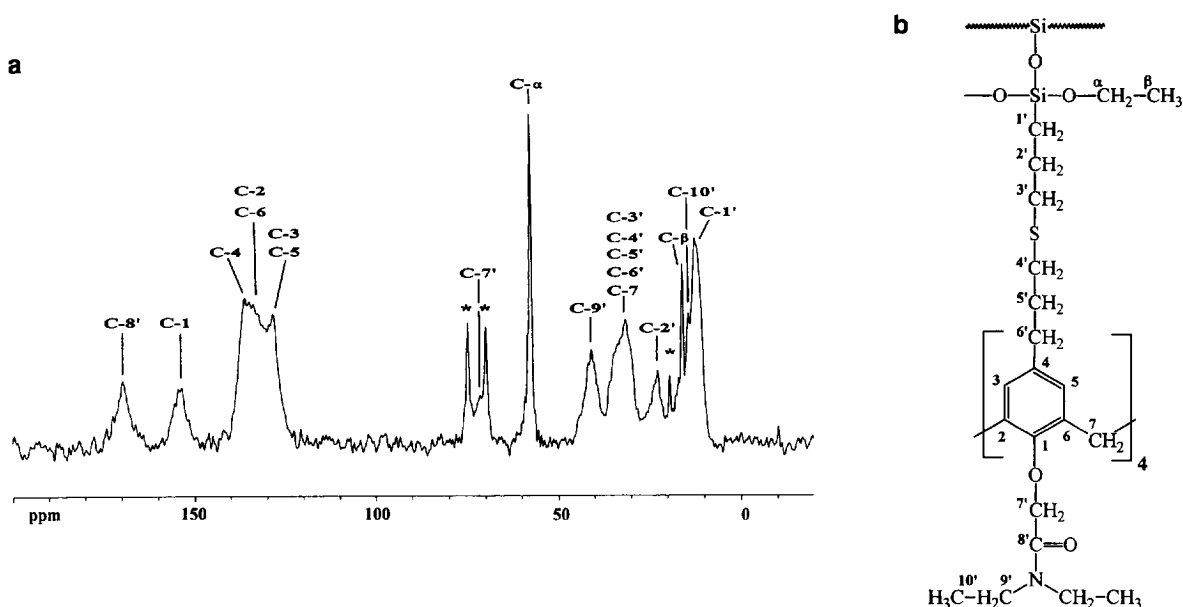


Fig. 5. (a) ^{13}C CP/MAS NMR spectrum of silica-bonded calixarene phase A. (b) Structure and assignment of the bonded calix[4]arene tetraamide phase A.

to the silica surface. The peaks of the thioalkyl spacer additionally to the peak of C-7 appear in the region between 10 and 45 ppm and can partially be resolved. Remaining ethoxy groups of the triethoxyalkylsilane give peaks at 16 and 58 ppm; these peaks possess a small linewidth due to the high mobility of the ethoxy groups. The peaks marked by an asterisk cannot be assigned to the structure of the calixarene. The sharpness of these lines suggest that the corresponding groups are high moveable, perhaps they arise from solvent molecules which are strongly adsorbed on the surface.

Silica bonded calixarene phase B has a similar carbon loading as phase A, nevertheless the signal to noise ratio of the ^{13}C CP/MAS NMR spectrum shown in Fig. 6a is much worse than that of phase A although the spectra were recorded under same conditions. The peak group with the highest intensity in the NMR spectrum is due to the resonance of the methyl group of the immobilized methylsilane. Therefore most of the carbon loading of phase B is due to the bonded methylsilane. The splitting of this peak indicates that a part of the methylsilane has not reacted; the methyl group of this unreacted silane with a direct bonded hydrogen shows a highfield

shift in relationship to the methyl group of the silane which has undergone hydrolysis or hydrosilylation addition reaction.

The intensity pattern of the signals of the calixarene carbon atoms of silica bonded calixarene phase B is quite different in comparison to that of phase A. The signal of the C-1' carbon atom of the alkyl spacer is weaker than the signals of the aromatic carbons. This fact and the presence of the signals of the unreacted allyl group (C-1a' and C-2a' in Fig. 6) indicate that the calixarene is not bonded over all spacers to the surface. The consequence of this weak bonding is a higher mobility of the calixarene which causes a less efficient magnetization transfer from the hydrogens to the carbons during cross polarization so that the signal intensity decreases.

4. Conclusions

^{13}C and ^{29}Si CP/MAS solid-state NMR is a very powerful method for synthesis control and characterization of chemically bonded stationary phases for chromatography. Direct evidence for the chemical attachment of macrocyclic calixarenes to silica has

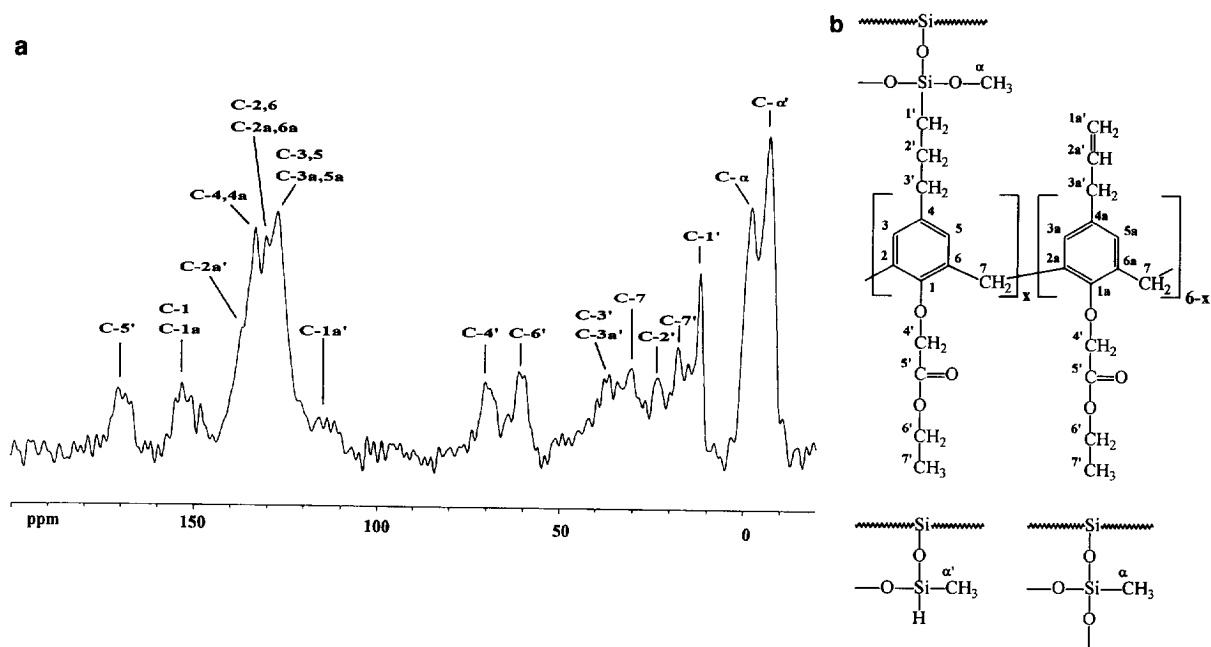


Fig. 6. (a) ^{13}C CP/MAS NMR spectrum of silica-bonded phase B. (b) Molecular structure and assignment of the carbon atoms of silica-bonded calix[6]arene hexaester.

been provided. In addition, for the particular experimental conditions and calixarenes here outlined, it is shown that the bonding of the calixarenes was more effective using the standard organosilane reaction than using hydride silica. With further work on the optimisation of the latter reaction scheme, this situation could be expected to change. The modification of the silica surface with dimethoxymethylsilane leads to a high amount of trifunctional methylsilane groups but in this case only to a small part of the wanted hydrosilylation product.

Acknowledgments

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