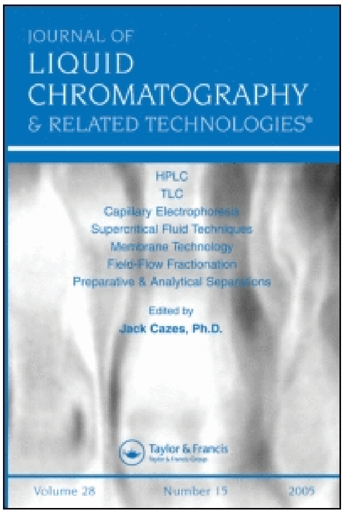

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Adamantyl Modified Silica via Olefin Hydrosilation on a Hydride Intermediate

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ABSTRACT

Adamantyl-containing reversed phase (RP) bonded materials were prepared by applying catalytic olefin hydrosilylation as the main surface modification reaction. Reversed phases containing adamantyl groups attached to the silica surface through ethyl and propyl moieties were prepared in this work. The corresponding olefins, namely 1-vinyladamantane (adamantyl-ethene) and 1-allyladamantane (3-adamantyl-propene) are not commercially available, and therefore, they were synthesized prior to the hydrosilation reaction. Infrared and nuclear magnetic resonance (NMR) characterizations of the olefins, and more importantly, those of the resulting bonded phases confirmed success of the reactions. Finally,

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the chromatographic characterization of the bonded phases, with special emphasis on the separation of basic solutes, was performed. A comparison of the separation performance of the new bonded materials with that obtained from conventional organosilanization is also an important part of the present work. The comparison has been extended to a C_{18} bonded phase to further emphasize the relationship between solute retention and the chemical nature of the modified silica surfaces.

Key Words: HPLC; Silica hydride; Silanization.

INTRODUCTION

One of the most commonly used approaches for the preparation of reversed phase (RP) supports involves the use of dimethylalkyl silanes of the type $XSiMe_2R$, where X is an easily hydrolyzable group (i.e., halide, alkoxy, acyloxy, etc.). This monofunctional organosilane (i.e., with only one X-group) produces a monomeric phase when reacted with silica, as shown in Eq. (1). The organic moieties are covalently attached to the silica substrate through a siloxane linkage (Si—O—SiC):

$$\mathrm{Si{-}OH} + \mathrm{XSiMe_2R} \longrightarrow |\mathrm{Si{-}O{-}SiMe_2R} + \mathrm{HX} \qquad (1)$$

The dimethylsiloxane structures not only function as anchor groups but also shield the remaining silanol groups on the surface of silica-based RP packing materials, which often interact strongly with the nitrogen lone pair electrons of basic solutes (many pharmaceutical compounds) and are very undesirable for that reason.

A number of approaches have been attempted to minimize silanol-related problems. One approach involves “end capping” the remaining silanols of the modified support with a smaller organosilane reagent, usually trimethylchlorosilane or hexamethyldisilazane. This results in a reduction in the concentration of surface silanols left unreacted by the primary bonding reaction. Since not all of the silanols are removed, this approach does not provide a total solution to the problem, although improvements in peak symmetry can be obtained. A second approach involves the use of mobile phase additives, such as alkylammonium salts, that reduce the concentration of accessible silanols by strongly adsorbing on them. Various mobile-phase additives have been tested as silanol blocking or masking agents. However, they do not solve the problem completely. A third approach involves reducing silanol accessibility via steric exclusion of the solute from the surface. It has been observed, that for a given type of bonded phase, the influence of residual silanols becomes less important as the alkyl chain length is increased. Longer alkyl chains partially prevent solutes from reaching the silica surfaces by physically shielding the underlying silanols. When the molecular features of an anchored group can enhance its shielding effect, a more hydrophobic surface can be obtained. Kirkland et al.[1] used "bidentate" organosilanes of the type $XSiR_2—Y—R_2SiX$. They also replaced the methyl group of the reagent in the reaction[1] by a bulkier one such as a secondary propyl or a tertiary butyl. Bidentate silanes containing one reactive site on each of the two terminal silicon atoms can form more than one covalent bond attached to the silica substrate, while the bridging Y group (—O—, $—CH_2CH_2—$, etc.) shields the underlying siloxane linkages. Monofunctional silanes containing two bulky groups on the silicon atom can also provide steric protection to the siloxane bond on the surface of the silica support. Additionally, both approaches show a significant increase in the stability of the bonded-phase packings.

The concept of steric shielding is also tested by the immobilization of moieties containing adamantyl groups. Adamantane (tricyclo [3.3.1.1.] decane) is a hydrocarbon containing 10 carbon atoms arranged in a completely symmetrical, three-dimensional structure in which four chair forms of cyclohexane are present and all bridgehead hydrogen atoms are equatorial with respect to each of the rings. This unique structure of adamantane results in an extremely rigid, relatively strain free chair conformation.[2]

Adamantyl-containing moieties have been attached to silica surfaces through a short and flexible hydrocarbon spacer arm. Such a bonded material can be pictured as a hydrocarbon-ball structure. A typical example is depicted in Fig. 1.

Adamantyl-bonded silica has been designed to reduce silanol accessibility by steric exclusion of the solute from the surface. The superior shielding properties of the adamantyl-modified surface arise from its structural rigidity compared to other surfaces modified with linear or slightly branched chains, which exhibit conformationally more dynamic structures and permit easier access to silanols. On the basis of the molecular size of adamantane (~7.5 Å diameter) and assuming a close pack structure, it has been suggested that the surface density can reach a maximum of 3.0–3.2 μmol/m^2.[2]

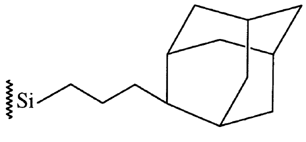
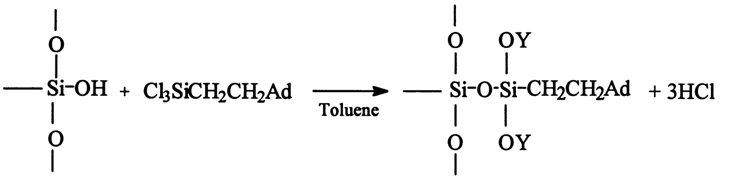


Figure 1. An adamantane-modified support.

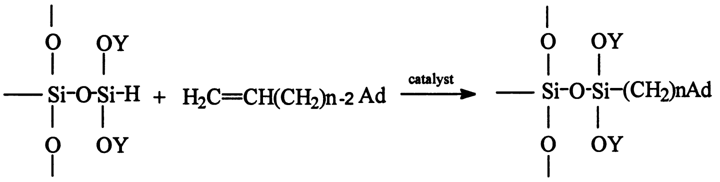
The surface that is chromatographically available is covered by ball-like adamantyl molecules, which block the underlying silanols left by the bonding reaction. Although some spaces between bonded ligands might still exist, most solutes, except for very small molecules (e.g., benzene, ~7 Å), will be blocked from reaching the surface silanols.[2]

Adamantyl-bonded silicas have been prepared so far by the use of conventional reaction of silicas with trifunctional adamantyl-containing organosilanes. More specifically, adamantylethylsilyl-silicas are made according to Ref.[2]—reaction 2:



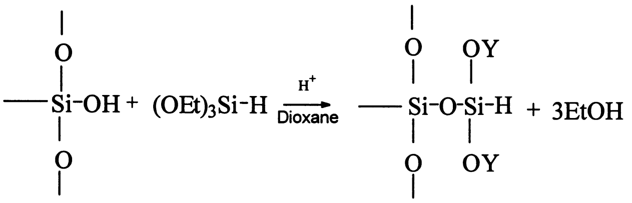
$$-\underset{\underset{|}{\mathrm{O}}}{\overset{\overset{|}{\mathrm{O}}}{\mathrm{Si}}}{-}\mathrm{OH} + \mathrm{Cl_3SiCH_2CH_2Ad} \xrightarrow[\text{Toluene}]{} -\underset{\underset{|}{\mathrm{O}}}{\overset{\overset{|}{\mathrm{O}}}{\mathrm{Si}}}{-}\mathrm{O}{-}\underset{\mathrm{OY}}{\overset{\mathrm{OY}}{\mathrm{Si}}}{-}\mathrm{CH_2CH_2Ad} + 3\mathrm{HCl} \qquad (2)$$

where Ad represents the adamantyl group. Pesek et al.,[3–7] have developed another approach for the preparation of bonded stationary phases. The method uses olefin hydrosilation as the main surface bonding reaction. The process seems quite well suited for the preparation of adamantyl-bonded phases.



$$-\underset{\underset{|}{\mathrm{O}}}{\overset{\overset{|}{\mathrm{O}}}{\mathrm{Si}}}{-}\mathrm{O}{-}\underset{\mathrm{OY}}{\overset{\mathrm{OY}}{\mathrm{Si}}}{-}\mathrm{H} + \mathrm{H_2C{=}CH(CH_2)_{n-2}\,Ad} \xrightarrow{\text{catalyst}} -\underset{\underset{|}{\mathrm{O}}}{\overset{\overset{|}{\mathrm{O}}}{\mathrm{Si}}}{-}\mathrm{O}{-}\underset{\mathrm{OY}}{\overset{\mathrm{OY}}{\mathrm{Si}}}{-}\mathrm{(CH_2)_nAd} \qquad (3)$$

The silicon-hydride-modified silica can readily be prepared by hydrosilanization of silica with the hydrolysis product of triethoxysilane (TES) as follows:



$$-\underset{\underset{|}{\mathrm{O}}}{\overset{\overset{|}{\mathrm{O}}}{\mathrm{Si}}}{-}\mathrm{OH} + \mathrm{(OEt)_3Si{-}H} \xrightarrow[\text{Dioxane}]{\mathrm{H^+}} -\underset{\underset{|}{\mathrm{O}}}{\overset{\overset{|}{\mathrm{O}}}{\mathrm{Si}}}{-}\mathrm{O}{-}\underset{\mathrm{OY}}{\overset{\mathrm{OY}}{\mathrm{Si}}}{-}\mathrm{H} + 3\mathrm{EtOH} \qquad (4)$$

where Y represents —H or —Si≡. By changing the value of *n* in Eq. (3), one can prepare a variety of adamantyl phases with spacer arms of different lengths. Naturally, the length should be long enough to provide a satisfactory surface attachment of the bulky ligands, but not too long as to lose the rigidity of the chemisorbed ball-like moieties. A logical value for n is 2 because it provides a bonded phase equivalent to that previously reported.[2] In this work, a second n value of 3 is also used.

EXPERIMENTAL

Reagents and Materials

All chemicals used, including 1-adamantaneethanol (98%), 1-bromoadamantane, allyl bromide (99%), anhydrous aluminum chloride, zinc dust, toluene, *o*-xylene, *m*-xylene, and carbon disulfide were purchased from Aldrich Chemical Co. (Milwaukee, WI). A 100 mM hexachloroplatinic acid (37.5% as Pt, Aldrich Chemical Co., Milwaukee, WI) solution in 2-propanol and *bis*-(triphenyl phosphine)-Ni(II) chloride were used as catalysts for hydrosilation. Phenol, caffeine, aniline, *N*,*N*-dimethylaniline (*N*,*N*-DMA), *N*,*N*-diethylaniline (*N*,*N*-DEA), norephedrine, and ephedrine were purchased from Aldrich Chemical Co. (Milwaukee, WI) and used as test solutes. In addition, 95% ethanol (Gold Shield Chemical Co., Hayward, CA) was used as received, and *p*-dioxane (J. T. Baker Chemical Co. Phillipsburg, NJ) was dried with calcium hydride (Sigma Chemical Co., St. Louis, MO) for several days and distilled before use. Triethoxysilane (Petrarch Systems Silanes & Silicones, Bristol, PA) was used as received. Bonded phases were prepared from Nucleosil 300-5 silica (lot #9201) and 300-7 silica (lot #1021), which were obtained from Macherey-Nagel (Düren, Germany). The relevant physical properties of the Nucleosil silica are shown in Table 1. Polycyclic aromatic hydrocarbons were obtained from the National Institute of Standards and Technology (Gaithersburg, MD). HPLC-grade methanol, acetonitrile, sodium chloride, and toluene were purchased from EM Sciences (Gibbstown, NJ). Boric acid, phosphoric acid, monobasic sodium phosphate, and dibasic sodium phosphate were purchased from J. T. Baker Chemical Co. (Phillipsburg, NJ). De-ionized (DI) water was obtained from a Milli-Q™ purification system (Millipore Corp., Bedford, MA).

Instrumentation

Differential Scanning Calorimetry

Differential scanning calorimetry (DSC) thermograms were obtained under atmospheric conditions with a Perkin-Elmer Model DSC-7 instrument.

Table 1. Silica physical properties and surface coverage of the bonded phases used in this study.

HPLC column	Type[a] (bonding)	Lot no.	Specific surface area (m^2/g)	Particle size mean diameter (μm)	Pore size mean diameter (nm)	Coverage ($\mu mol/m^2$)
$C{-}C_{18}$	Conventional	1,021	100.00	7	30.0	2.31
C—AdE	Conventional ad-ethyl	9,201	95.2	5	42.9	3.27
H—AdE	Via hydride ad-ethyl	9,201	95.2	5	42.9	2.19
H—AdP	Via hydride ad-propyl	9,201	95.2	5	42.9	3.49
H	Hydride	9,201	95.2	5	42.9	

[a] Conventional, bonded phase prepared by organosilanization; via hydride, bonded phase prepared via hydride intermediate; ad, adamantyl.

Approximately 5 mg of adamantyl-ethylborate was loaded into a platinum pan and heated to 500°C at a rate of 20°C/min for the analysis.

Infrared Spectrometry

Fourier-transform infrared (FT-IR) spectra for vinyl- and allyladamantane samples were obtained on a Perkin-Elmer Model 1800 FT-IR spectrometer. Neat liquid samples were examined between two KBr salt plates without a spacer.

A Perkin-Elmer Model 1800 FT-IR spectrometer equipped with a deuterated triglycine sulfate (DTGS) detector was used for diffuse reflectance infrared Fourier transform (DRIFT) spectra. A Spectra-Tech^{TM} DRIFT accessory equipped with a sample cup (3 mm diameter and 2 mm depth) was used for analysis. KBr was finely ground, dried for several hours in an oven at 110°C, and then an equal amount (by weight) of silica sample was added and mixed. The mixtures were placed in the DRIFT sample cup. A microscope slide was pressed down onto the cup with a circular motion to obtain a smooth sample surface. Spectra were collected in the 4000–450 cm^{-1} region with a nominal resolution of 2 cm^{-1}, using one hundred sample scans rationed against KBr as a reference, and the spectra were normalized to 100% transmittance.

Elemental Analysis

A Perkin-Elmer Model 240C elemental analyzer equipped with a Perkin-Elmer Model 56 recorder was used for the carbon analysis of the bonded silicas. For each analysis, 2 to 5 mg of sample was used.

Nuclear Magnetic Resonance

Proton and carbon nuclear magnetic resonance (NMR) spectra were obtained on a General Electric Model QE 300 (300 MHz) instrument for identification of adamantane bonded phases. The NMR measurements were performed using 10 μL of sample dissolved in 1 mL deuterated chloroform ($CDCl_3$) solvent in a 5-mm o.d. glass tube. Proton chemical shifts were referenced to the peak of $CDCl_3$, which was at 7.24 ppm from tetramethylsilane (TMS). Carbon-13 shifts were referenced to the solvent $CDCl_3$ triplet peaks at 76.59, 77.02, and 77.44 ppm from TMS.

Solid state NMR spectra with cross polarization (CP) and magic angle spinning (MAS) were obtained on a 300-MHz Bruker Model MSL 300 spectrometer. Magic angle spinning was obtained at a spinning rate of 5 kHz, and 300 to 500 mg of bonded silica sample was placed in a double bearing ZrO_2 rotor. ^{13}C CP-MAS NMR spectra were recorded with a pulse width of 6.5 μs, a contact time of 5 ms, and a pulse repetition rate of 5 sec. ^{29}Si CP-MAS NMR spectra were recorded with a pulse width of 12 μs, a contact time of 5 ms, and a pulse repetition rate of 5 sec.

Liquid Chromatography

Evaluation of columns was performed with a Hewlett-Packard (Avondale, PA) Model 1050 liquid chromatograph system equipped with a quaternary gradient pump, an automatic injector, a variable wavelength UV detector, and a PC-based data station. Stainless steel tubes (15 cm × 0.46 cm i.d., Alltech Co., Deerfield, IL) were used for column packing with a Haskel pneumatic pump (Burbank, CA) operated at 6000 psi with methanol as the driving solvent.

Procedures

Preparation of Adamantyl-Substituted Terminal Olefins

Vinyladamantane

First, a 14.056 g (0.227 mol) portion of boric acid was added to a solution of 41.0 g (0.227 mol) of 1-adamantaneethanol in 700 mL of toluene. The mixture was refluxed for 42 hours and a trap was used to provide for permanent water separation (8.1 mL collected). Toluene was removed by distillation. Adamantyl-ethylborate was pyrolyzed at 415°C, while the 1-vinyladamantane product (22.064 g) was collected (b.p. 224°C at atmospheric pressure). The product was further purified by vacuum distillation (b.p. 78–79°C at 2 mmHg) and a clear liquid was obtained. A viscous brown residue (probably poly-vinyl-adamantane) remained after distillation.

Allyladamantane

First, 1-bromoadamantane and anhydrous aluminum chloride were measured in a glove bag under dry nitrogen gas. Zinc dust was activated upon brief contact with 10% HCl followed by thorough rinsing with DI water. Dry ice with *o*-xylene was used at −30°C and −70°C in thermally isolated cups. Then, 9.11 g of anhydrous aluminum chloride (0.068 mol) was slowly added to 196 g of 1-bromoadamantane (0.91 mol) and 78.8 mL allyl bromide (0.91 mol) in carbon disulfide at −70°C. Afterwards, the temperature was increased to −30°C and maintained at that level for approximately 1 hour. The reaction mixture was then poured into about 500 mL of crushed ice and magnetically stirred until all the ice melted. After extraction with ether, the extracts were washed with DI water and dried over magnesium sulfate. After the removal of ether by distillation, 1-(2,3-dibromopropyl) adamantane was obtained.

At this point, a 79.6 g portion of activated zinc dust was slowly added to a mixture of 700 mL of 95% ethanol and the 1-(2,3-dibromopropyl) adamantane product. The reaction mixture was refluxed for 24 hours with vigorous stirring. At the end of this period, the mixture was cooled down and poured into 500 mL of DI water and extracted with ether. The ether extracts were washed with water and dried over magnesium sulfate. The ether was then removed by distillation and the 1-allyladamantane was purified by vacuum distillation (b.p. 59–61°C at 0.8–0.9 mmHg). A colorless liquid of 1-allyladamantane (150.02 g) was collected.

Preparation of Bonded Phases

Bonded Phases Via Hydride Intermediate

Silanization with Triethoxysilane (TES). First, a 14.00-g portion of dry silica was weighted into a 500-mL, 3-neck round bottom flask equipped with a condenser, a thermometer, an equalizing addition funnel, and a magnetic stirring bar. Then 30.8 mL of 1.0 M TES/dioxane solution was transferred through a cannula to the addition funnel, and 237 mL of reagent-grade dioxane was added to the silica, followed by 12.2 mL of 2.3 M HCl. The mixture was then heated to 70 ± 5°C. The TES/dioxane solution was added dropwise with vigorous stirring. Then, the temperature was raised to a full reflux and the reaction was allowed to proceed for 90 min. After a cooling period, the reaction mixture was centrifuged (5 min at 1000–1500 rpm), washed twice with 150-mL portions of 75% (v/v) THF/water, and then washed twice with 150-mL portions of 75% (v/v) THF/diethyl ether. The final product was dried at room temperature overnight to evaporate the ether and, finally, dried in a vacuum oven at 110°C for several hours.

Olefin Hydrosilylation. Prior to hydrosilation, all the glassware used was dried in an oven at 110°C while the silica hydride was dried under vacuum at this temperature and then stored in a desiccator. A 40-mL portion of 1-allyladamantane was transferred to a round bottom flask, followed by 200 μL of 100 mM hexachloroplatinic acid solution in 2-propanol. This mixture was heated at 100 ± 2°C for 44 hours with magnetic stirring. After this "induction" period, a clear solution was obtained. Then, 4.00 g of hydride silica was slowly added (in approximately 15–20 min) to the olefin/catalyst solution. The reaction was allowed to proceed for 76 hours at 100 ± 2°C. After a cooling period, the bonded silica product was centrifuged and washed with four 30-mL portions of benzene, followed by similar washings with dichloromethane and diethyl ether. The final solvent was allowed to evaporate at room temperature overnight and the product was then dried under vacuum at 60°C for 6 hours.

A similar procedure was used for vinyl-adamantane. Additionally, an equimolar amount of 13.08 mg of *bis*-(triphenyl phosphine)-Ni(II) chloride was used as an alternate catalyst with both olefins. Unlike the Pt catalyst, a completely clear solution was not obtained with the Ni catalyst under the conditions used.

Conventional Bonded Phase by Organosilanization. First, a 4.00-g portion of dried silica was transferred into a clean, dry, 100-mL, three-neck round bottom flask equipped with a condenser and a magnetic stirrer. Then, 40 mL of carbon tetrachloride, 2.2 mL of adamantylethyltrichloro silane, and 165 μL of DI water were sequentially added with vigorous stirring. The reaction mixture was refluxed for 5 hours. After the reaction mixture was cooled down to room temperature, the product was washed two times with 50-mL portions of carbon tetrachloride to remove excess silane reagent. The solid was further washed with carbon tetrachloride/methanol 1:1 v/v (one time), methanol (one time), methanol/water 1:1 v/v (three times), methanol (two times), and diethyl ether (two times). The reaction product was dried at room temperature overnight and finally at 60°C under vacuum overnight.

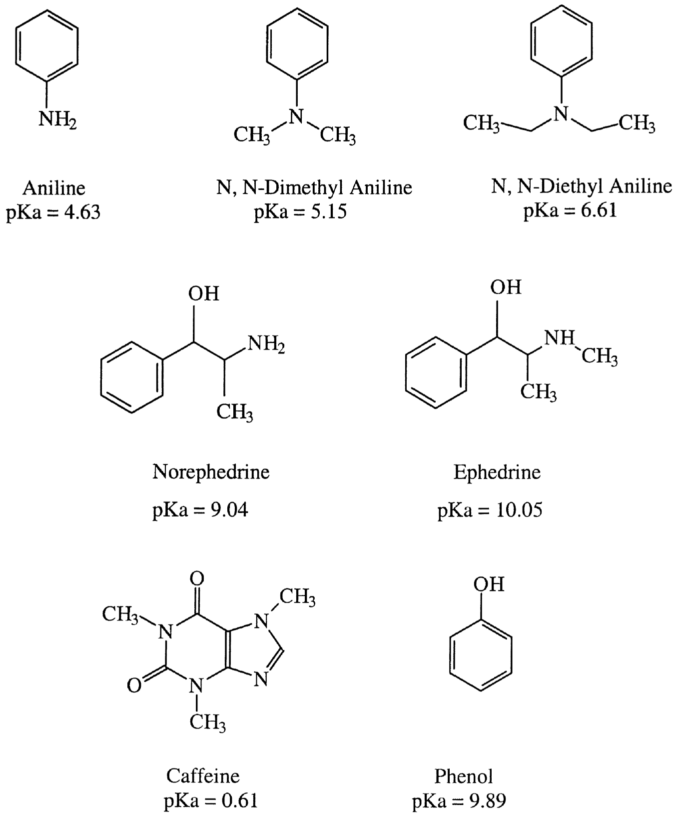
HPLC Separation

Polycyclic Aromatic Hydrocarbon

The column void volume was measured using 0.01 mM KNO_3 as an unretained marker. Standard Reference Material (SRM) 869, containing three polycyclic aromatic hydrocarbons (PAHs): benzo[a]pyrene (BaP), 1,2:3,4:5,6:7,8-tetrabenzo naphthalene (TBN), and phenanthro[3,4-c]phenenthrene (PhPh), was used to test the selectivity of the different adamantyl-bonded phases. HPLC separations were isocratically performed in acetonitrile/water at 2 mL/min at ambient column temperature with an injection volume of 10 μL. Detection was at 254 nm.

Basic Solutes

Phenol, as a polar non-basic solute (0.1 mM) along with caffeine, aniline, *N*,*N*-dimethylaniline, *N*,*N*-diethylaniline, norephedrine, and ephedrine as basic probes, were separated isocratically on octadecyl and adamantyl phases. Figure 2 shows the structures and the pKa values of the seven basic test solutes and phenol. Solutes were dissolved in the mobile phase (i.e., 55% v/v methanol in water). The flow rate was 1.5 mL/min with an injection volume of 5 μL and the detection wavelength was set at 210 nm. Basic probes were



Aniline
pKa = 4.63

N, N-Dimethyl Aniline
pKa = 5.15

N, N-Diethyl Aniline
pKa = 6.61

Norephedrine
pKa = 9.04

Ephedrine
pKa = 10.05

Caffeine
pKa = 0.61

Phenol
pKa = 9.89

Figure 2. Structures and pKa values of seven basic test solutes and phenol.

isocratically separated on octadecyl and adamantyl phases with 55% (v/v) methanol and 45% phosphate buffer at pH 2 and at pH 7.

RESULTS AND DISCUSSION

Olefin and Bonded Phase Syntheses

Vinyladamantane

First, 1-vinyladamantane was prepared according to the procedure developed by O'Conner et al.,[8] by esterification of adamantane-ethanol with boric acid in refluxing toluene followed by pyrolysis of the resulting borate. A very low yield was obtained when the pyrolysis was carried out at the temperature reported in Ref.[8] (270°C). Therefore, it was decided to run a thermal scan using DSC as shown in Fig. 3. This figure confirms that no significant amount of decomposition occurred at 270°C. Increasing the temperature up to 500°C showed an endothermic peak at 420°C (onset 414°C) as shown in the insert of Fig. 3. This strongly suggests that the pyrolysis temperature should be around 415°C. An isothermal scan (not shown) at 415°C showed an endothermic decomposition, which appeared to be completed after about 10 min at this temperature, as shown in Fig. 3. When metaborate trimer was pyrolyzed at 415°C, a 59.0% yield of 1-vinyladamantane was obtained. Figure 4 shows the reaction scheme for the preparation of 1-vinyladamantane.

In the FT-IR spectrum obtained from 1-vinyladamantane after purification by vacuum distillation there are several strong peaks at 3080 cm^{-1} (olefin C—H stretching vibration), 1640 cm^{-1} (C=C stretching mode of unconjugated olefin), and peaks at 995 cm^{-1}, 905 cm^{-1}, and 814 cm^{-1} (out-of-plane C—H bending vibration modes). It is evident that the most characteristic bands are those from the vinyl group. In addition, a strong peak at 1450 cm^{-1} is an indication of the C—H bending vibration of cyclohexane. Finally, a weaker peak is observed in the 1350–1150 cm^{-1} region, which indicates an absorption of a hydrocarbon due to methylene twisting and wagging vibrations.[9]

The distribution of protons in the NMR spectrum, as shown by the integration curves, represents a total of 18 hydrogens. Peak assignments[10] are given in Table 2.

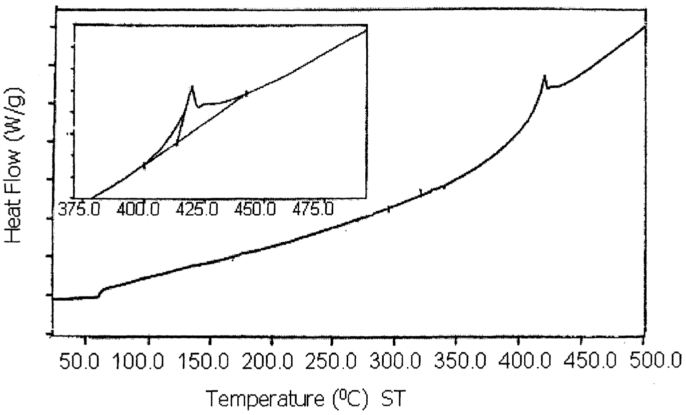


Figure 3. DSC curves of adamantyl-ethyl-borate.

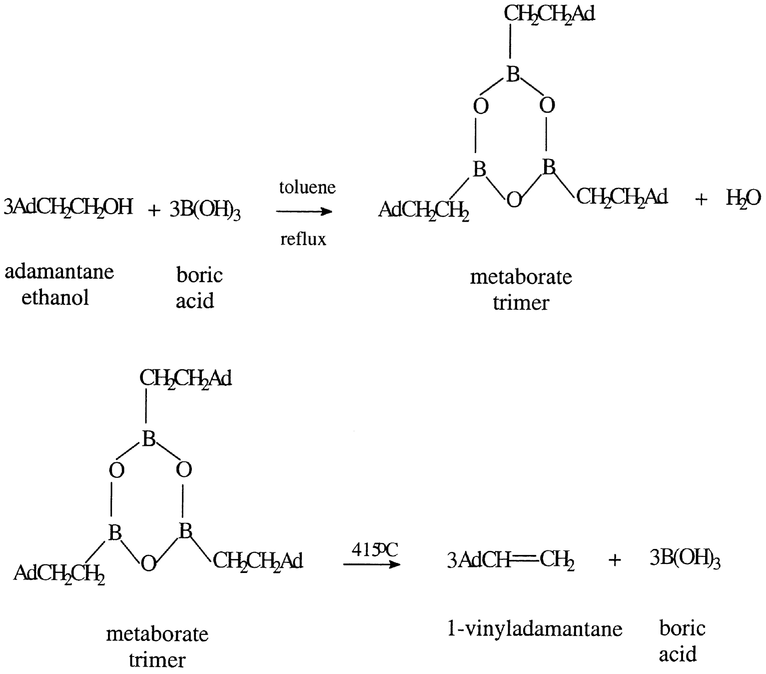


Figure 4. Reaction scheme for the preparation of 1-vinyladamantane.

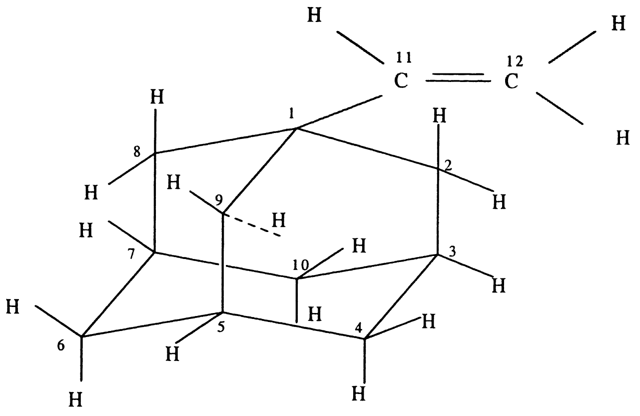
^{13}C NMR analysis provides conclusive confirmation for the terminal $=CH_2$ structure. The two downfield ^{13}C peaks are clearly due to vinyl groups, and the peak at 149.99 ppm can, therefore, be assigned to carbon #11 and the peak at 108.93 ppm can be assigned to carbon #12. The remainder of peak assignments is given in Table 2.

Allyladamantane

1-Allyladamantane was prepared according to the procedure developed by Calpaldi et al.[11] involving the reaction of 1-bromoadamantane and allyl bromide in carbon disulfide at $-70°C$ in the presence of anhydrous aluminum chloride. Dehalogenation of the product with zinc gave a final yield of 94.6% of 1-allyladamantane. The reaction scheme for the preparation of 1-allyladamantane is shown in Fig. 5.

The FT-IR spectrum of 1-allyladamantane is similar to 1-vinyladamantane. The ^{1}H NMR spectrum shows the presence of the allylic methylene group. The ^{1}H NMR spectrum of 1-allyladamantane can be assigned in a similar manner to

Table 2. Proton and carbon NMR chemical shifts for 1-vinyladamantane.



1-Vinyladamantane

^{1}H NMR		^{13}C NMR	
Hydrogen	ppm	Carbon	ppm
11 (1H)	5.70	11 (1C)	149.99
12 (2H)	4.86	12 (1C)	108.93
2, 8, 9 (6H)	1.68	2, 8, 9 (3C)	41.86
4, 6, 10 (6H)	1.56	4, 6, 10 (3C)	36.92
3, 5, 7 (3H)	1.96	3, 5, 7 (4C)	28.46
		1 (1C)	35.48

that of 1-vinyladamantane, except the two protons of the allyl group attached to carbon #13 are responsible for the peak at 1.82 ppm. Also the ^{13}C NMR spectrum of 1-allyladamantane can be used to confirm the presence of the allyl group attached to the adamantane molecule. The proton and carbon NMR chemical shifts of 1-allyladamantane are summarized in Table 3.

Bonded Phases

The concentration of surface-bonded groups, α_R, was calculated from the carbon content of the bonded material and the Brunauer, Emmet, and Teller

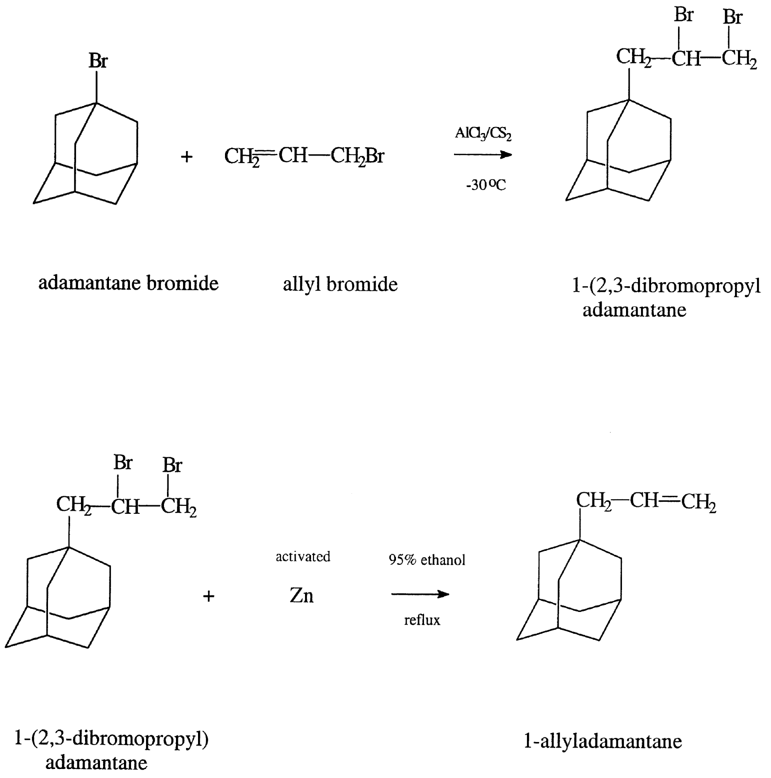


Figure 5. Reaction scheme for the preparation of 1-allyladamantane.

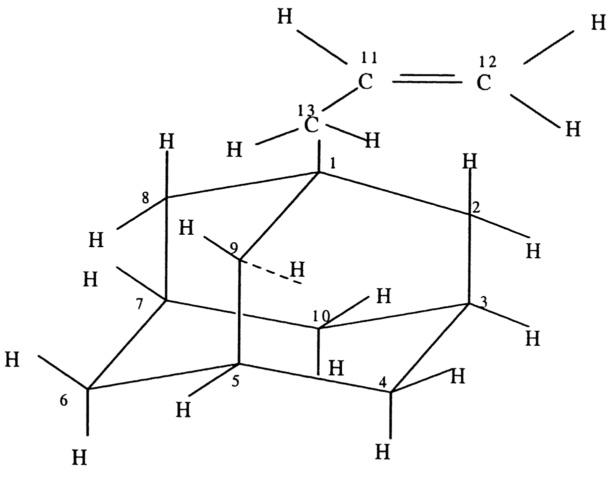
(BET) specific surface area of the native silica before bonding. The following equation proposed by Berenden and de Galan[12] was used:

$$\alpha_{\mathrm{R}}(\mu\mathrm{mol/m^2}) = \frac{10^6 p_c}{(10^2 M_{\mathrm{c}} n_{\mathrm{c}} - p_{\mathrm{c}} M_{\mathrm{R}})} S_{\mathrm{BET}} \tag{5}$$

where p_{c} is the carbon percentage of the bonded material (by weight after correction from any carbon present before bonding), M_{c} is the atomic weight of carbon, n_{c} is the number of carbon atoms in the bonded organic group, M_{R} is the molecular weight of the attached group, and S_{BET} is the specific surface area of the native substrate. The physical properties and the surface coverage for the different bonded silica-based packings in this study are shown in Table 1.

Different spectroscopic methods including DRIFT, ^{13}C and ^{29}Si CP-MAS NMR were used to prove that the olefin undergoes Si—H addition at the silica

Table 3. Proton and carbon NMR chemical shifts for 1-allyladamantane.



l-Allyladamantane

^{1}H NMR		^{13}C NMR	
Hydrogen	ppm	Carbon	ppm
11 (1H)	5.8	11 (C)	134.82
12 (2H)	5.0	12 (1C)	116.47
2, 8, 9 (6H)	1.64	2, 8, 9 (3C)	42.40
4, 6, 10 (6H)	1.48	4, 6, 10 (3C)	37.14
3, 5, 7 (3H)	1.95	3, 5, 7 (3C)	28.77
13 (2H)	1.80	13 (1C)	49.08
		1 (1C)	32.65

surface. Also, the hydride intermediate and the conventional adamantyl-ethyl silica were analyzed via DRIFT and CP-MAS NMR. Figure 6 compares DRIFT spectra of (A) hydride Nucleosil and (B) adamantyl-propyl on hydride Nucleosil. The silanization product of hydride Nucleosil (curve A) shows the presence of an Si—H stretching band at 2260 cm^{-1}. The observation of strong C—H stretching vibration peaks between 2800 cm^{-1} and 3000 cm^{-1} in curve B confirms the presence of adamantyl-propyl on hydride Nucleosil. It is not surprising that there is a strong peak due to Si—H stretching in curve B, since this bonded phase was prepared from the hydride intermediate. Figure 7 compares (A) adamantyl-ethyl silica prepared by the conventional method and (B) adamantyl-ethyl on hydride

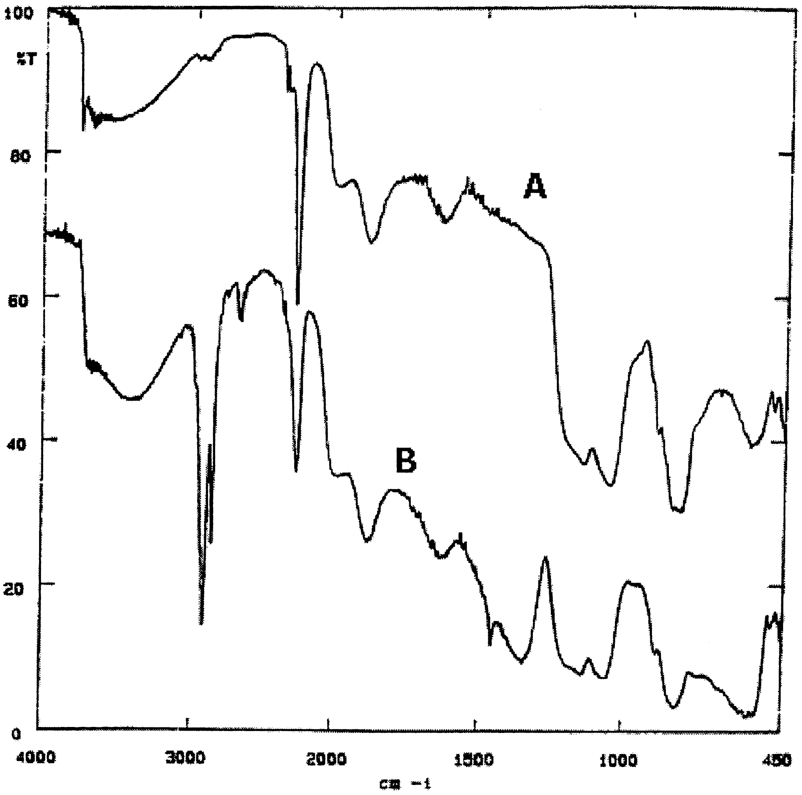


Figure 6. DRIFT spectra of (A) hydride Nucleosil and (B) adamantyl-propyl on hydride Nucleosil.

Nucleosil prepared by hydrosilation. Adamantyl-ethyl-bonded silica prepared by the conventional method only shows the C—H stretching bands between 2800 cm^{-1} and 3000 cm^{-1}, since no Si—H stretching is possible by this method.[4,5] Additionally, these results suggest that both the adamantyl ethyl and adamantyl propyl were bonded to the silica surface.

Solid state NMR spectroscopy offers another way of proving that the olefins undergo Si—H addition at the silica surface. Figure 8 shows the ^{13}C CP-MAS NMR spectra of (A) adamantyl-ethyl silica prepared by the conventional method, (B) adamantyl-ethyl on hydride Nucleosil, and (C) adamantyl-propyl on hydride Nucleosil. The strongest peak near 29 ppm can be assigned to carbons 3, 5, 7, and the strong peak at 42 ppm is due to carbons 2, 8, 9. The peak at 37 ppm can be assigned to carbons 4, 6, 10.[9] There is no

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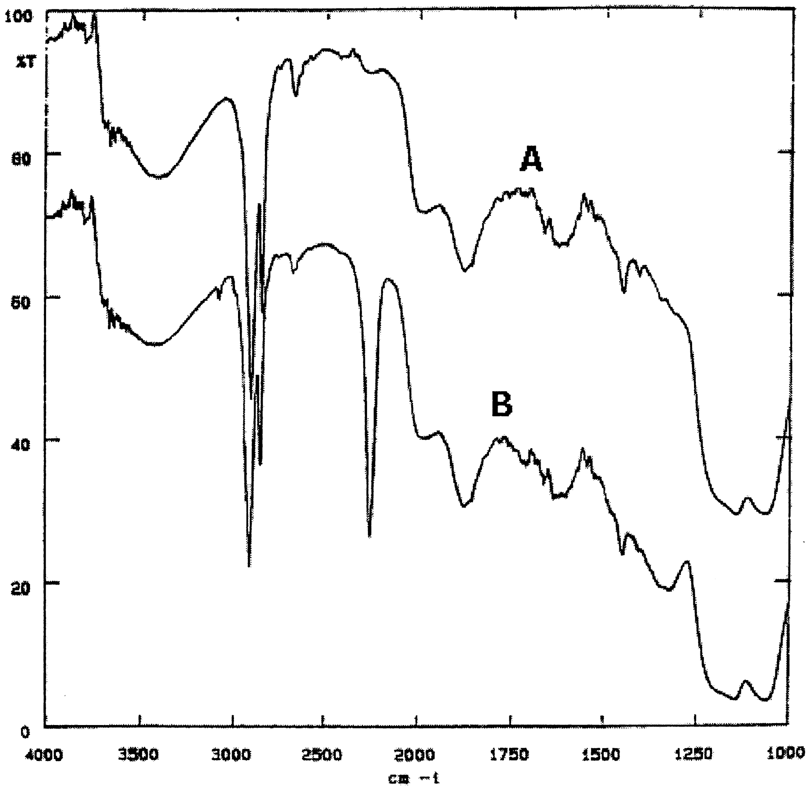

Figure 7. DRIFT spectra of (A) adamantyl-ethyl silica prepared by the conventional method and (B) adamantyl-ethyl on hydride Nucleosil prepared by hydrosilylation.

evidence in the spectrum of the terminal olefin peak after bonding to silica. The terminal olefin group is involved in the direct bonding on the hydride Nucleosil in the hydrosilylation reaction.

Figure 9 (curve A) shows the ^{29}Si CP-MAS NMR spectrum of adamantyl-ethyl silica prepared by the conventional method. The peak at −110 ppm represents the framework of Si*(OSi≡)$_4$ structures, the peak at −99.5 ppm represents surface single silanols, HOSi*(OSi═)$_3$, while the peaks at −56 ppm and −46.5 ppm can be assigned to CSi*(OSi═)$_3$ and C(HO)— Si*(OSi═)$_2$, respectively.[4,5] Curve B shows the ^{29}Si CP-MAS NMR spectrum for adamantyl-ethyl Nucleosil prepared using the hydride intermediate. The peaks at −110 ppm and −99.5 ppm are as described above. The peak at −63.5 ppm represents the Si*(OSi≡)$_3$C moiety on the surface, while the one at

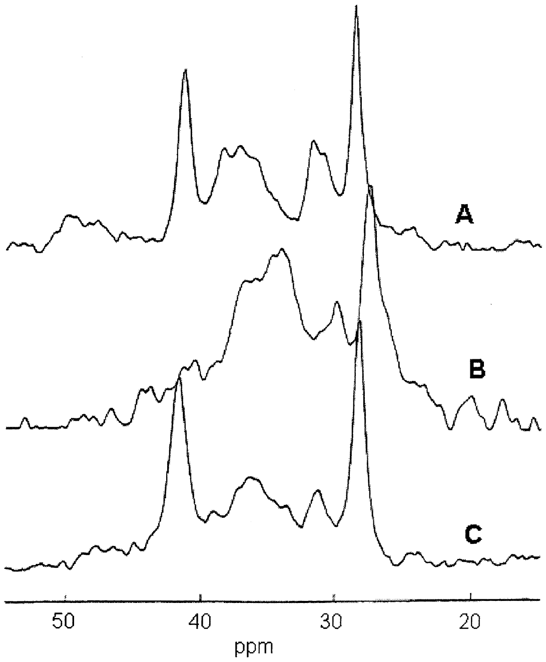

Figure 8. The ^{13}C CP-MAS NMR spectra of (A) adamantyl-ethyl silica prepared by the conventional method, (B) adamantyl-ethyl on hydride Nucleosil, and (C) adamantyl-propyl on hydride Nucleosil.

-84.0 ppm is due to the hydride, $Si^*(OSi\equiv)_3H$. Curve C shows the ^{29}Si CP-MAS NMR spectrum for adamantyl-propyl Nucleosil prepared using the hydride intermediate. The two peaks at -110 ppm and -100 ppm are as described above. It is not surprising that the same peak at -84 ppm due to the hydride $H\text{-}Si^*(OSi\equiv)_3$ species is seen here, since the bonded phase was prepared from the hydride. The last peak at -65.2 ppm, which represents $CSi^*(OSi\equiv)_3$, clearly indicates that the terminal olefin group is directly attached to the surface silicon atom.

HPLC Performance

Polycyclic Aromatic Hydrocarbons

Sander and Wise proposed the use of NIST Standard Reference Material (SRM) 869 to characterize LC columns. A classification scheme for different

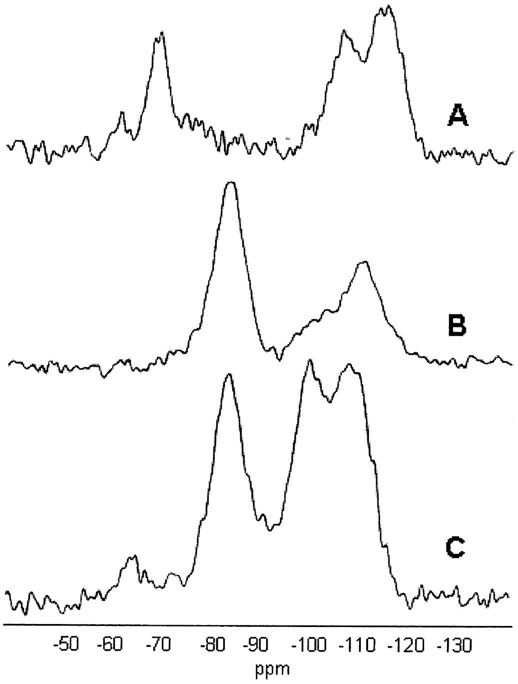

Figure 9. The ^{29}Si CP-MAS NMR spectrum of (A) adamantyl-ethyl silica prepared by the conventional method and (B) adamantyl-ethyl Nucleosil prepared using the hydride intermediate.

types of phases has been proposed based on the elution order of these three components. Monomeric C_{18} phases, prepared with monofunctional silane reagents, are characterized by the following elution order: BaP $\leq$ PhPh $<$ TBN. Polymeric C_{18} phases, prepared with trifunctional silanes show the elution order PhPh $<$ TBN $\leq$ BaP. Phases with intermediate properties, heavily loaded monomeric or lightly loaded polymeric C_{18} phases, give the elution order PhPh $<$ BaP $<$ TBN.[13–15] Comparisons among different C_{18} phases can be established from the selectivity factor of TBN with respect to BaP, $\alpha_{\mathrm{TBN/BaP}}$, as defined by Eq. (6) below.

$$\alpha_{\mathrm{TBN/BaP}} = \frac{k'_{\mathrm{TBN}}}{k'_{\mathrm{BaP}}} \tag{6}$$

Values for $\alpha_{\mathrm{TBN/BaP}}$ are less than 1.0 for polymeric phases and greater than 1.7 for monomeric phases. Table 4 lists the results obtained from different

Table 4. Retention and selectivity data for the three-component standard SRM 869 on octadecyl and adamantyl Nucleosil silicas.

	k'			
Silica	BaP	PhPh	TBN	$\alpha_{\mathrm{TBN/BaP}}$
C—C_{18}Nucleosil (conventional)	3.70	3.92	6.30	1.69
C—Ad-ethyl Nucleosil (conventional)	1.86	2.32	3.43	1.83
H—Ad-ethyl Nucleosil (from hydride)	1.50	1.75	2.33	1.54
H—Ad-propyl Nucleosil (from hydride)	1.90	2.31	3.50	1.84

alkyl-adamantyl and octadecyl-bonded phases used in this study. An elution order of BaP < PhPh < TBN was observed on all the columns, and the selectivity factor of TBN with respect to BaP ($\alpha_{\mathrm{TBN/BaP}}$) was measured to be greater than 1.5, which is similar to that observed for the conventional monomeric C_{18} phase.

Octadecyl and adamantyl-ethyl phases from hydride showed a similar selectivity factor even though they have different molecular structures. The selectivity factors obtained were similar for the conventional adamantyl-ethyl and adamantyl-propyl Nucleosil (from hydride) despite the difference in alkyl chain length and preparation methods.

Basic Solutes

Basic compounds can elute with asymmetric peaks and poor column efficiency in HPLC separations. The problems are due to the strong interaction of the basic nitrogen functionality with the residual silanol groups on the surface. This is not surprising since a significant number of silanols remain on alkyl-bonded phases. The surface concentration of the smallest modifier group available, i.e., trimethylsilyl, is about 4.7 μmol/m^2 under optimum conditions. However, the presence of bulky groups, such as phenyl on the organosilane, drastically reduces the possible surface coverage to as low as 2.5 μmol/m^2. In this study, the concept of steric shielding was tested by the immobilization of moieties containing adamantyl groups. The surface that is chromatographically available is covered by ball-like adamantyl molecules, which block the underlying silanols left after the bonding reaction. The superior shielding properties of the adamantyl-modified surface arise from its structural rigidity compared to other surfaces modified with linear or slightly branched chains, which exhibit conformationally more dynamic structures, and hence, permit easier access to silanols.

The methodology employed in this work combines the mobile phase conditions and some probes used by Engelhard et al.[16,17] with the mobile phase buffering at acidic and neutral pH conditions utilized by Tanaka et al.[18] Similarly, basic probes with pKa values above nine were also included in this work. Caffeine, with a low pKa value, is very poorly protonated at low pH conditions, but essentially uncharged at a neutral pH value. As a result, this solute is a good probe for the examination of hydrogen-bonding interactions at low pH values. Aniline, *N*,*N*-DMA and *N*,*N*-DEA are small solutes with medium pKa values. They exhibit low (aniline and *N*,*N*-DMA) to moderate (*N*,*N*-DEA) protonation at neutral pH conditions, and therefore, show correspondingly weak electrostatic interactions under these conditions. On the other end are norephedrine and ephedrine. Because of their high pKa values, these solutes are extensively protonated (above 90%) at neutral pH, and therefore, are extremely sensitive to electrostatic interactions with ionized silanols.

Naturally, the dissociation behavior of the surface silanols must also be considered. The pKa value of the most acidic silanol groups on amorphous silica has been shown to be about 7.1.[19] The fully hydroxylated surface of silica has a point of zero charge near pH 2.[19] Upon increasing the pH, ionization increases slowly up to pH 6 and then increases rapidly up to pH 10.7. However, above pH 8 or 9, the silica framework starts dissolving and forms silicate ions.[19]

Throughout this work, 55% v/v methanol/buffer ($\mathrm{pH} = 2$ or $\mathrm{pH} = 7$) was used as the mobile phase, a condition under which the reversed phase material is completely wetted by the alcohol while the water content is still sufficient for extensive polar interactions. Under these conditions, hydrogen-bonding effects for uncharged solutes and ion-exchange effects for ionic solutes can be independently assessed. In this study, a total of five columns were tested, those listed in Table 1 and the hydride intermediate [as shown in Eq. (4)] is also included in some cases. It should be pointed out that, due to the minimal size of the hydride species, any silanols presents will be completely unshielded, and hence, readily available for both hydrogen-bonding and ion-exchange interactions.

In Table 5, relative selectivity factors of basic test solutes with respect to phenol on five columns are listed with a mobile phase at $\mathrm{pH} = 2$ and $\mathrm{pH} = 7$. At pH 2, all basic solutes except caffeine are 90% or more in the protonated form, while at pH 7, only those with pKa of 9 or higher remain in this form. The values (less than one) at low pH indicate that caffeine eluted before phenol in all columns except the hydride and ethyladamantyl phase. The results at low

Table 5. The effect of surface chemistry on the relative selectivity[a] factor of basic test solutes with respect to phenol at two different pH values (see Table 1 for column identification).

Test sample	Column	pH = 2	pH = 7	Test sample	Column	pH = 2	pH = 7
Caffeine	$C{-}C_{18}$	0.42	0.43	Aniline	$C{-}C_{18}$	0.45	0.75
	C—AdE	0.78	0.82		C—AdE	0.25	0.90
	H—AdE	1.41	1.30		H—AdE	0.60	1.00
	H—AdP	0.90	1.10		H—AdP	0.55	0.95
	H	1.80	1.65		H	0.85	1.20
N,*N*-DMA	$C{-}C_{18}$	0.50	5.50	*N*,*N*-DEA	$C{-}C_{18}$	0.50	20.00
	C—AdE	0.50	3.95		C—AdE	0.51	10.00
	H—AdE	1.50	2.30		H—AdE	3.00	4.50
	H—AdP	0.60	3.10		H—AdP	1.00	7.50
	H	2.50	1.50		H	4.00	3.00
Nor-Ephedrine	$C{-}C_{18}$	0.30	2.35	Ephedrine	$C{-}C_{18}$	0.50	7.50
	C—AdE	0.35	2.50		C—AdE	0.60	6.00
	H—AdE	0.65	4.70		H—AdE	1.00	9.00
	H—AdP	0.50	2.60		H—AdP	0.90	5.90
	H	0.70	7.10		H	1.20	13.50

[a] $\alpha_{B/P} = (k'_{\text{base}}/k'_{\text{phenol}})$.

Note: All data are an average of triplicate experiments.

pH conditions (no high selectivity values of caffeine with respect to phenol) indicate that there is very little hydrogen bonding on all phases. The relatively high selectivity of the adamantyl-ethyl phase (made by silianization reaction of hydride Nucleosil silica) for some solutes may be associated with the lower surface coverage of the organic group. The lower surface coverage allows the smaller phenol molecule to penetrate further into the bonded phase network than the larger basic compounds. Therefore, the relative separation between them increases.

The fact that many of the test solutes eluted before, or co-eluted with phenol at low pH, indicates negligible contribution from hydrogen bonding. For example, aniline eluted before phenol in all columns at both acidic and neutral pH conditions. The only exception is the hydride phase at neutral pH, with a $\alpha_{B/P}$ value slightly above 1. Therefore, the selectivity of aniline appears to be independent of the surface chemistry. The relative selectivity behavior of bases with moderate pKa values, i.e., *N*,*N*-DMA and *N*,*N*-DEA, shows that the conventional C_{18} exhibits the greatest ion-exchange interactions. The strong retention of *N*,*N*-DEA, as evidenced by high $\alpha_{B/P}$ values, agrees with similar findings by our research group.[3,4] When compared with other phases, the hydride showed relatively strong hydrogen-bonding interactions and relatively weak ion-exchange interactions with the tested solutes. When basic solutes with high pKa values (i.e., >9) are considered (specifically norephedrine and ephedrine), it is the hydride column that shows the strongest ion-exchange interactions with these solutes. In the case of *N*,*N*-DMA and *N*,*N*-DEA, no significant shielding at $\text{pH} = 7$, appeared to be furnished by the conventional C-AdE and hydride H-AdP adamantyl columns.

Peak asymmetry features were also analyzed to evaluate the properties of the adamantyl-silica phases prepared via hydride and by the conventional method. The peak asymmetry is calculated by the A/B ratio at 50% of the peak height. In Table 6, this parameter for several basic solutes eluted at pH 2 and 7 are shown. The hydride phase (i.e., the one with the minimal shielding) shows symmetric peaks, even for the high pKa solutes. Some examples of chromatograms of basic compounds on the hydride phase are shown in Fig. 10. Improvement of peak symmetry for some solutes can also be observed for the H—AdE phase as compared to the conventional C_{18} phase.

The "real" test for silanophilic interactions is at neutral pH conditions where all silanols, if present, are ionized and can interact with cationic solutes. At $\text{pH} = 7$, in the case of all solutes except *N*,*N*-DEA, the results closest to 1 (most symmetrical peaks) were obtained for the H-AdE phase. In fact, only ephedrine on the C—AdE phase had an undesirable asymmetry factor (>1.5).

It should be noted, that these findings agree with those of Gilpin et al.,[2] and disagree with those of Aubel et al.[20] In Aubel's work, the polar effect observed on the adamantane phase was due to very low surface coverage of the

Table 6. The effect of surface chemistry on the asymmetry[a] of basic test solutes at two different pH values (see Table 1 for column identification).

Test sample	Column	pH = 2	pH = 7	Test sample	Column	pH = 2	pH = 7
Caffeine	C—C_{18}	1.00	1.00	Aniline	C—C_{18}	1.00	1.05
	C—AdE	1.00	1.05		C—AdE	1.00	1.00
	H—AdE	1.00	1.00		H—AdE	1.00	1.00
	H—AdP	1.00	1.00		H—AdP	1.00	1.10
	H	1.05	1.00		H	1.00	1.05
N,*N*-DMA	C—C_{18}	1.10	1.05	*N*,*N*-DEA	C—C_{18}	1.15	1.20
	C—AdE	1.00	1.00		C—AdE	1.00	1.10
	H—AdE	1.00	1.00		H—AdE	1.00	1.05
	H—AdP	1.00	1.00		H—AdP	1.00	1.25
	H	1.00	1.00		H	1.00	1.00
Nor-Ephedrine	C—C_{18}	1.00	1.15	Ephedrine	C—C_{18}	1.10	1.35
	C—AdE	1.10	1.15		C—AdE	1.05	2.00
	H—AdE	1.00	1.00		H—AdE	1.00	1.07
	H—AdP	1.00	1.08		H—AdP	1.00	1.30
	H	1.00	1.10		H	1.00	1.15

[a] A/B ratio at 50% of the peak height.

Note: All data are an average of triplicate experiments.

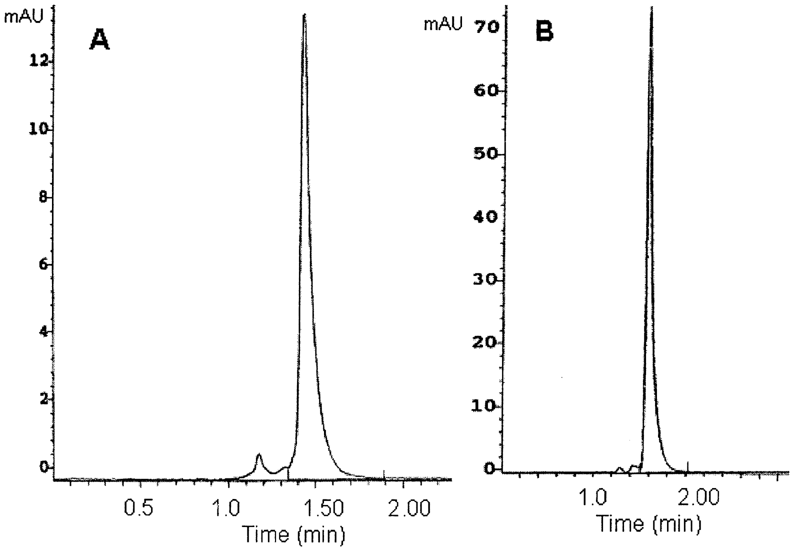

Figure 10. Chromatograms of basic compounds on the hydride bonded stationary phase. (A) *N*-diethylaniline and (B) ephedrine. Conditions described in Experimental section.

bonded phase used (prepared from adamantylethylchlorosilane). The HPLC data obtained during the course of this work show that good shielding of the surface silanols was provided by the H—AdE bonded phase even though it had the lowest surface coverage of stationary phases tested (see Table 1). This result emphasizes the effect of the hydride layer in removing most of the accessible silanols and providing a surface suitable for the analysis of basic compounds.

CONCLUSIONS

It has been demonstrated that adamantyl containing hydrocarboneous/ phases can be readily prepared by catalytic hydrosilylation of vinyl-modified adamantanes on a hydride substrate. As expected, the RP HPLC behavior of the new phases appeared to be similar to that of "regular" C_{18} phases. When basic solutes were used as test probes, the bulky ball-like adamantyl groups and the underlying hydride surface seem to be able to effectively shield any unreacted silanol groups to prevent the latter from interacting with the basic probes. The RP behavior of PAH compounds in the adamantyl silicas was similar to that of a monomeric C_{18} phase.

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