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Adamantyl silica for RP-HPLC via olefin hydrosilation on a hydride intermediate

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**ADAMANTYL SILICA FOR RP-HPLC
VIA OLEFIN HYDROSILATION ON A HYDRIDE INTERMEDIATE**

A Thesis

Presented to

The Faculty of the Department of Chemistry

San Jose State University

In Partial Fulfillment

of the Requirements for the Degree

Master of Science

by

Susan Tong

July, 1995

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ABSTRACT

ADAMANTYL SILICA FOR RP-HPLC VIA OLEFIN HYDROSILATION ON A HYDRIDE INTERMEDIATE

by Susan Tong

The preparation and chromatographic evaluation procedures of adamantyl-bonded silica-based stationary phases for high performance liquid chromatography (HPLC) are described. The silica modification procedure follows a previously established method consisting of the catalytic hydrosilylation of terminal olefins on a hydride-modified intermediate to obtain ethyl- and propyl-adamantyl bonded packings. 1-Vinyladamantane is prepared by pyrolysis of the borate ester of 1-adamantane-ethanol. 1-Allyladamantane is prepared by the adduction of 1-bromo-adamantane and allyl-bromide, and the product is dehalogenated with zinc. Columns are evaluated by using several selected probes including polycyclic aromatic hydrocarbons, as well as selected basic compounds. No significantly improved silanol shielding appears to be provided by the structurally rigid adamantyl groups compared to the dynamic linear C₁₈ moieties.

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1. INTRODUCTION

1.1. Background

Reversed phase (RP), the most popular mode of high performance liquid chromatography (HPLC), is usually carried out on a wide variety of linear alkyl-bonded silica-based stationary phases. Butyl (C_4), octyl (C_8) and octadecyl (C_{18}) phases are commonly used for these separations because of their excellent selectivity towards many solutes, ranging from low molecular-weight organic solutes such as polycyclic aromatic hydrocarbons (PAHs) to biological macromolecules such as proteins. Many pharmaceutical compounds are basic in nature, a fact that often leads to low efficiency and asymmetry peaks in RP-HPLC separations. These problems are associated with residual silanol groups on the surface of silica-based RP packing materials which often interact strongly with the nitrogen lone pair electrons of the basic solutes. It is now widely accepted that at least half of the total surface silanols remain underivatized after exhaustive organosilanization. The remaining silanols are left unbonded as a result of non ideal reaction conditions, steric hindrance from groups already bonded to the surface, or inaccessibility of silanols to the bonding reagent.

Currently, one of the most commonly used approaches for the preparation of 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 equation 1. The organic moieties are covalently attached to the silica substrate through a siloxane linkage (Si-O-SiC):

The dimethylsiloxane structures not only function as anchor groups but also shield the remaining silanol groups.

In a similar approach, trifunctional organosilanes, X_3SiR , are used to prepare polymeric bonded phases. The organosilane can react with neighboring silanes as well as the silica surface, creating a polymeric organic layer:

where X is as defined above and Y represents -H or -Si≡. Due to the steric hindrance of the R group, both reactions 1 and 2 cannot go to completion, and hence, residual acidic silanols remain in varying degrees on the surface of the alkyl-bonded silicas.

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. In a recent report, Kirkland et al. [1] used “bidentate” organosilanes of the type $\text{XSiR}_2\text{-Y-R}_2\text{SiX}$. They also replaced the methyl group of the reagent in 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 ($-\text{O}-$, $-\text{CH}_2\text{CH}_2-$, etc.) shields the underlying siloxane linkages. Monofunctional silanes containing two bulky groups on the

silane 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. This is pictorially shown in Figure 1 [1].

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 ten carbon atoms arranged in a completely symmetrical, three-dimensional molecule 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 support can be pictured as a hydrocarbon-ball field. A typical example is depicted in Figure 2.

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 mmole/m² [2].

Figure 1. Schematic representation of the bonding of bidentate and monofunctional silanes to a hydroxylated surface.

Figure 2. 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 according to reaction (2). More specifically, adamantylethylsilyl-silicas are made according to [3]:

where Ad represents the adamantyl group. Recently Sandoval et al. [3, 4, 5, 6] developed a new approach for the preparation of bonded stationary phases. The method uses olefin hydrosilylation as the main surface bonding reaction. The process seems quite well suited for the preparation of adamantyl-bonded phases.

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

where Y is defined as in reaction 1 above. By changing the value of n in equation 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.

1.2. Aims of this work

One major goal of the present research is to prepare adamantyl-containing RP bonded phases by applying catalytic olefin hydrosilylation as the main surface bonding reaction. More specifically, adamantyl groups attached to the silica surface through ethyl and propyl are prepared in this work. This corresponds to n values in equation 3 of 2 and 3 for ethyl and propyl, respectively. The corresponding olefins, namely 1-vinyladamantane (adamantyl-ethene) and 1-allyladamantane (3-adamantyl-propene) are not commercially available, and therefore, their syntheses are necessary. IR and NMR characterizations of the olefins, and more importantly, those of the resulting bonded material are also important aspects of this work. Finally, the chromatographic characterization of the bonded phases, with special emphasis on the separation of basic solutes, is another major goal of the present research. A comparison of the separation performance of the new bonded materials with that obtained from the conventional organosilanization (equation 2a) is also an important part of the present work. The comparison has been extended to the more familiar C_{18} bonded phases, to further emphasize the relationship between solute retention and the chemical nature of the modified silica surfaces.

2. EXPERIMENTAL

2.1. 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 hydrosilylation. Phenol, caffeine, aniline, N,N-dimethylaniline, N,N-diethylaniline, norephedrine, ephedrine and amitriptyline 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 used. 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). LC-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

(D. I.) water was obtained from a Milli-Q™ purification system (Millipore Corp., Bedford, MA).

Table 1. Physical properties of silica support materials used in this work

Brand name	Lot number	Particle size Mean diameter (μm)	Pore size Mean diameter (nm)	Specific surface area (m^2/g)
Nucleosil 300-5	9201	5	42.9	95.2
Nucleosil 300-7	1021	7	30	100
Nucleosil 300-10	0051	10	38.8	75.35

2.2. Instrumentation

2.2.1. Differential Scanning Calorimetry

Differential scanning calorimetry (DSC) thermograms were obtained in room atmosphere with a Perkin-Elmer Model DSC-7 instrument. Approximately 5 mg of adamantyl-ethylborate was loaded into a platinum pan and heated up to 500 °C at a rate of 20 °C/min for the analysis.

2.2.2. Infrared Spectrometry

Fourier-transform infrared (FT-IR) spectra for vinyl- and allyl-adamantane 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™ 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 mixed. The mixtures were filled to 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} , with one hundred sample scans ratioed against KBr as reference, and the spectra were normalized to 100% transmittance.

2.2.3. Elemental Analysis

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

2.2.4. Nuclear Magnetic Resonance

Proton and carbon NMR spectra were obtained on a General Electric Model QE 300 (300 MHz) instrument for identification of vinyl and allyl-adamantane. The NMR measurements were performed using 10 μ L 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 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. MAS was obtained at a spinning rate of 5 kHz and 300 to 500 mg of bonded silica sample was measured in a double bearing ZrO_2 rotor. ^{13}C CP-MAS NMR spectra were recorded with a pulse width of 6.5 μ s, 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 μ s, a contact time of 5 ms and a pulse repetition rate of 5 sec.

2.2.5. 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 x 0.46 cm i.d., Alltech Co., Deerfield, IL) were used for

column packing with a Haskel pneumatic pump (Burbank, CA) operated at 6,000 psi with methanol as the driving solvent.

2.3. Procedures

2.3.1. Preparation of Adamantyl-Substituted Terminal Olefins

2.3.1.1. 1-Vinyladamantane

First, a 14.056-g (0.227-mole) portion of boric acid was added to a solution of 41.0 g (0.227 mole) 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 mm Hg) and a clear liquid was obtained. A viscous brown residue (probably poly-vinyl-adamantane) remained after distillation.

2.3.1.2. 1-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 D.I. 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 mole) was slowly added to 196 g of 1-bromoadamantane (0.91 mole) and 78.8 mL allyl bromide (0.91 mole) 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 D. I. 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 D. I. 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 mm Hg). A colorless liquid of 1-allyladamantane (150.02 g) was collected.

2.3.2. Preparation of Bonded Phases

2.3.2.1. New Bonded Phases via Hydride Intermediate

2.3.2.1.1. Silanization with 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 minutes. After a cooling period, the reaction mixture was centrifuged (5 minutes at 1,000-1,500 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.

2.3.2.1.2. Olefin Hydrosilylation

Prior to hydrosilylation, 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 μ L 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 minutes) 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 110 °C for 6 hours.

A similar procedure was used for vinyl-adamanatane. 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.

2.3.2.2. 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 μ L of D. I. 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 110 °C under vacuum overnight.

2.3.4. HPLC Separation

2.3.4.1. Polycyclic Aromatic Hydrocarbon

The column void volume was measured using 0.01 mM KNO₃ 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]phenanthrene (PhPh), was used to test the selectivity of the different adamantyl-bonded phases. Figure 3 shows the structures of the three PAH components in SRM 869. 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.

2.3.4.2. Basic Solutes

Phenol as a polar non-basic solute (0.1 mM) along with caffeine, aniline, N,N-dimethylaniline, N,N-diethylaniline, norephedrine, ephedrine and amitriptyline as basic probes were separated isocratically on octadecyl and adamantyl phases. Figure 4 shows the structures and the pK_a 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 isocratically separated on octadecyl and adamantyl phases with 55% (v/v) methanol and 45% phosphate buffer at pH 2 and at pH 7.

BENZO[a]PYRENE

TETRABENZONAPHTHALENE

PHENANTHRO [3,4-C] PHENNANTHREN

Figure 3. Structures of the PAH components in SRM 869.

Figure 4. Structures and pK_a values of seven basic test solutes and phenol.

3. RESULTS AND DISCUSSION

3.1. Olefin and Bonded Phase Syntheses

3.1.1. 1-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 reference 8. Therefore, it was decided to run a thermal scan using DSC as shown in Figure 5a. 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 Figure 5b. 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 minutes at this temperature as shown in Figure 5a. When metaborate trimer was pyrolyzed at 415 °C, a 59.0% yield of 1-vinyladamantane was obtained. Figure 6 shows the reaction scheme for the preparation of 1-vinyladamantane.

Figure 7 shows the FT-IR spectrum obtained from 1-vinyladamantane after purification by vacuum distillation. Based on several strong peaks at 3080 cm^{-1} (olefin C-H stretching vibration), 1640 cm^{-1} (C=C stretching mode of unconjugated olefin), and the

Figure 5 a. DSC curves of adamantyl-ethyl-borate

Figure 5 b. DSC curve of adamantyl-ethyl-borate.

Figure 6. Reaction scheme for the preparation of 1-vinyladamantane

Figure 7. FTIR spectrum of 1-vinyladamantane

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 $1350\text{-}1150\text{ cm}^{-1}$ region which indicates an absorption of a hydrocarbon due to methylene twisting and wagging vibrations [9].

Figure 8 shows the ^1H NMR spectrum obtained from $10\text{ }\mu\text{L}$ of 1-vinyladamantane in a 1 mL deuterated chloroform (CDCl_3) solution. Proton chemical shifts were referenced to the CDCl_3 peak at 7.24 ppm from TMS. The distribution of protons as shown by the integration curves represents a total of 18 hydrogens. The peak at 5.7 ppm can be assigned to the proton attached to carbon atom # 11 and the peak at 4.86 ppm can be attributed to the two equivalent protons attached to carbon # 12 (see Table 2). Thus, it is evident that the vinylic group is attached to the adamantane molecule. Three protons attached to carbon # 3, 5 and 7 are responsible for the peak at 1.96 ppm . The peaks at 1.68 ppm and 1.56 ppm are due to the two sets of six protons each attached to carbons 2, 8, 9 and carbons 4, 6, 10, respectively [10].

The ^{13}C NMR spectrum of 1-vinyladamantane is shown in Figure 9. Carbon-13 shifts were referenced to the solvent CDCl_3 triplet peaks at 76.59 , 77.02 and 77.44 ppm from TMS. ^{13}C NMR analysis provides conclusive confirmation for the terminal $=\text{CH}_2$ 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 strong peak at 28.46 ppm must be the absorption from

carbons 3, 5, 7. The weakest peak at 35.48 ppm is due to the tertiary carbon # 1. The strongest peak at 41.86 ppm is due to carbons 2, 8, 9 and the peak at 36.92 ppm is due to carbons 4, 6, 10, respectively [10]. Proton and carbon NMR chemical shifts for 1-vinyladamantane are summarized in Table 2.

3.1.2. 1-Allyladamantane

1-Allyladamantane was prepared according to the procedure developed by Eugene 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 Figure 10.

Figure 11 shows the FT-IR spectrum of 1-allyladamantane which is similar to 1-vinyladamantane. The ^1H NMR spectrum (Figure 12) shows the presence of the allylic methylene group. The ^1H NMR spectrum of 1-allyladamantane can be assigned in a similar manner to 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 (Figure 13) 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.

Figure 8. Proton NMR spectrum of 1-vinyladamantane

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

1-Vinyladamantane

Proton NMR		Carbon NMR	
hydrogen	ppm	carbon	ppm
11 (1H)	5.7	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

Figure 9. Carbon NMR spectrum of 1-vinyladamantane

Figure 10. Reaction scheme for the preparation of 1-allyladamantane.

Figure 11. FT-IR spectrum of 1-allyldamantane.

Figure 12. Proton NMR spectrum of 1-allyladamantane

Figure 13. Carbon NMR spectrum of 1-allyladamantane

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

1-Allyldamantane

Proton NMR		Carbon 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

3.1.3. Bonded Phases

The concentration of surface-bonded groups, α_R , was calculated from the carbon content of the bonded material and the BET specific surface area of the native silica before bonding. The following equation proposed by Berenden and de Galan was used:

$$\alpha_R \text{ (}\mu\text{mole/m}^2\text{)} = 10^6 p_c / (10^2 M_c n_c - p_c M_R) S_{\text{BET}} \quad (5)$$

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 [5]. The physical properties and the surface coverage for the different bonded silica-based packings in this study are shown in Table 4.

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 surface. Also, the hydride intermediate and the conventional adamantyl-ethyl silica were analyzed via DRIFT and CP-MAS NMR. Figure 14 compares DRIFT spectra of (A) hydride Nucleosil and (B) allyladamantane on hydride Nucleosil. The silanization product of hydride Nucleosil (curve A) shows the presence of Si-H stretching band at $2,260 \text{ cm}^{-1}$. The observation of strong C-H stretching vibration peaks between $2,800 \text{ cm}^{-1}$ and $3,000 \text{ cm}^{-1}$ in curve B confirms the presence of allyl-adamantane on hydride Nucleosil. It is not surprising that

Table 4. Silica physical properties and surface coverage in this study.

Sample I.D.	Type* (bonding)	Lot no.	Surface area (m ² /g)	Particle diameter (μm)	Pore diameter (nm)	Surface coverage (μmole/m ²)
cC ₁₈	Conv. C ₋₁₈	1021	100	7.0	30	2.31
nC ₁₈	New C ₋₁₈	0051	75.35	10	38.85	4.42
cAE	Conv. Ad-ethyl	9201	95.2	5	42.9	3.27
nAE	New Ad-ethyl	9201	95.2	5	42.9	2.19
nAP	New Ad-propyl	9201	95.2	5	42.9	3.49
H	Hydride	9201	95.2	5	42.9	

*Conv., conventional bonded phase by organosilanization; New, new bonded phase via hydride intermediate; Ad, adamantyl.

there is a strong peak due to Si-H stretching in curve B, since this bonded phase was prepared from the hydride intermediate. Figure 15 compares (A) adamantyl-ethyl silica prepared by the conventional method and (B) vinyladamantane on hydride Nucleosil prepared by hydrosilylation. Adamantyl-ethyl-bonded silica prepared by the conventional method only shows the C-H stretching bands between $2,800\text{ cm}^{-1}$ and $3,000\text{ cm}^{-1}$, 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 16 shows the ^{13}C CP-MAS NMR spectra of (A) adamantyl-ethyl silica, (B) vinyladamantane on hydride Nucleosil, and (C) allyl-adamantane 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]. It is evident that there is no 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 17 (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 $\text{Si}^*(\text{OSi}\equiv)_4$ structures, the peak at -99.5 ppm represents surface single silanols, $\text{HOSi}^*(\text{OSi}\equiv)_3$, while the peaks at -56 ppm and -46.5 ppm can be assigned to $\text{CSi}^*(\text{OSi}\equiv)_3$ and $\text{C}(\text{HO})\text{-Si}^*(\text{OSi}\equiv)_2$, respectively [4,5]. Curve B shows the ^{29}Si CP-MAS NMR spectrum for adamantyl-ethyl Nucleosil prepared using the hydride intermediate.

Figure 14. DRIFT spectra of hydride-modified silicas: (A) hydride Nucleosil, (B) adamantyl-propyl on hydride Nucleosil.

Figure 15. DRIFT spectra of hydride-modified silicas: (A) adamantyl-ethyl on Nucleosil, (B) adamantyl-ethyl on hydride Nucleosil.

Figure 16. ^{13}C CP-MAS NMR spectra of Nucleosil silicas: (A) adamantyl-ethyl silica, (B) adamantyl-ethyl on hydride Nucleosil, and (C) adamantyl-propyl on hydride Nucleosil.

The peaks at -110 ppm and -99.5 ppm are as described above. The peak at -63.5 ppm represents the $\text{Si}^*(\text{OSi}\equiv)_3\text{C}$ moiety on the surface while the one at -84.0 ppm is due to the hydride, $\text{Si}^*(\text{OSi}\equiv)_3\text{H}$. 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 $\text{H-Si}^*(\text{OSi}\equiv)_3$ species is seen here since the bonded phase was prepared from the hydride. The last peak at -65.2 ppm, which represents $\text{CSi}^*(\text{OSi}\equiv)_3$, clearly indicates that the terminal olefin group is directly attached to the surface silicon atom.

3.4. HPLC Performance

3.4.1. Polycyclic Aromatic Hydrocarbons

Sander and Wise proposed the use of NIST Standard Reference Material (SRM) 869 to characterize LC columns. The test mixture consists of the following PAHs in acetonitrile: benzo[a]pyrene (BaP), 1,2:3,4:5,6:7,8-tetra-benzonaphthalene (TBN) also known as dibenzo[g,p]chrysene, and phenanthro[3,4-c] phenanthrene (PhPh). A classification scheme for different 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: $\text{BaP} \leq \text{PhPh} < \text{TBN}$. Polymeric C_{18} phases, prepared with trifunctional silanes show the elution order $\text{PhPh} < \text{TBN} \leq \text{BaP}$. Phases with intermediate properties, heavily loaded monomeric or lightly

Figure 17. ^{29}Si CP-MAS NMR spectra of Nucleosils: (A) adamantyl-ethyl silica, (B) adamantyl ethyl on hydride Nucleosil, and (C) adamantyl propyl on hydride Nucleosil.

loaded polymeric C₁₈ phases, give the elution order PhPh < BaP < TBN [12, 13, 14].

Comparisons among different C₁₈ phases can be established from the selectivity factor of TBN with respect to BaP, $\alpha_{\text{TBN/BaP}}$, as defined by equation 6 below.

$$\alpha_{\text{TBN/BaP}} = k'_{\text{TBN}} / k'_{\text{BaP}} \quad (6)$$

$$k' = (t_r - t_o) / t_o \quad (7)$$

where k' is the retention factor, t_r is the analyte retention time and t_o is the void volume.

Values for $\alpha_{\text{TBN/BaP}}$ are less than 1.0 for polymeric phases and greater than 1.7 for monomeric phases. Figures 18, 19 and 20 show typical chromatograms for the SRM869 mixture on different alkyladamantyl-bonded phases. Table 5 lists the results obtained from different alkyl-adamantyl-bonded phases 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 ($\alpha_{\text{TBN/BaP}}$) was measured to be greater than 1.5, which is similar to that observed for the conventional monomeric C₁₈ 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.

Figure 18. Typical HPLC separation profile for the SRM 869 mixture on the adamantyl-ethyl Nucleosil prepared by the conventional method. The mixture was separated isocratically using 85%/15% acetonitrile/water at a flow rate of 2 mL/min and detected at 254 nm. Component identification: 1, BaP; 2, PhPh; and 3, TBN.

Figure 19. Typical HPLC separation profile for the SRM 869 mixture on the adamantyl-ethyl Nucleosil prepared using hydride. Separation conditions and component identification are the same as in Figure 18.

Figure 20. Typical HPLC separation profile for the SRM 869 mixture on the adamantyl-propyl Nucleosil prepared using hydride. Separation conditions and component identification are the same as in Figure 18.

Table 5. Retention and selectivity data for the three-component standard SRM 869 on octadecyl and adamantyl Nucleosil silicas.

Silica type	BaP k'	PhPh k'	TBN k'	α TBN/BaP
C ₁₈ Nucleosil (conventional)	3.70	3.92	6.30	1.69
C ₁₈ Nucleosil (from hydride)	2.29	2.29	3.54	1.54
Ad-ethyl Nucleosil (conventional)	1.86	2.32	3.43	1.83
Ad-ethyl Nucleosil (from hydride)	1.50	1.75	2.33	1.54
Ad-propyl Nucleosil (from hydride)	1.90	2.31	3.50	1.84

3.4.2. Basic Solutes

Basic compounds generally elute with asymmetric peaks and poor column efficiency in HPLC separations. The problems are associated with 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. A surface concentration of the smallest modifier group available, i.e., trimethylsilyl, is about $4.7 \mu\text{mole}/\text{m}^2$ under optimum conditions [15]. However, the presence of bulky groups such as phenyl on the organosilane drastically reduces the possible surface coverage to as low as $2.5 \mu\text{mole}/\text{m}^2$. 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 9 were also included in this work. Structures and ionization constants for the probes used are shown in Figure 4. Caffeine, with a low pKa value, is very poorly protonated at low pH conditions, but essentially neutral (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 intense electrostatic interactions under these conditions. On the other end are norephedrine, ephedrine and amitriptyline. 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 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].

In the absence of mobile phase additives, a methanol eluent containing between 30% and 50% v/v of water should provide convenient retention of polar compounds on alkyl-modified silicas [16]. Throughout this work, we used 55% v/v methanol, a condition under which the reversed phase is completely wetted by the alcohol while the water content is still sufficient for extensive polar interactions. The problem with this mobile phase is that there is no pH control, and therefore, one cannot differentiate between the contributions from hydrogen-bonding effects and ion-exchange effects. Similar mobile

phases (55% v/v MeOH) buffering at pH 2 and pH 7, were preferentially used, so that hydrogen-bonding effects for uncharged solutes and ion-exchange effects for ionic solutes can be independently assessed. Figure 21 pictorially describes hydrogen-bonding and ion-exchange interactions between a basic solute and surface silanol groups at acidic and neutral pH conditions.

In this study, a total of six columns were tested. The types of bonded phase and their preparation methods are listed in Table 4. Conventional and new C₁₈ bonded phases are also included for comparison purposes. Additionally, the hydride intermediate (as shown in equation 4) is also included in some cases. It should be pointed out that, due to the minimal size of the hydride species, any silanol presents will be completely unshielded, and hence, readily available for both hydrogen-bonding and ion-exchange interactions.

Figure 22 shows the relative retention times of aniline, N,N-DEA and norephedrine with respect to phenol on different columns with an unbuffered mobile phase. The $\alpha_{B/P}$ values (i.e., k'_{base} / k'_{phenol}) of N,N-DEA and norephedrine are significantly higher compared to that of aniline. Amitriptyline showed strong adsorption on all columns without pH controls.

Figure 23 shows theoretical curves for the fraction of protonated base at various pH conditions for seven basic solutes. At pH 2, all basic solutes except caffeine are 90% or more in the protonated form, while at pH 7, only those with pK_a of 9 or higher remain in this form.

(A) Hydrogen-bonding in acidic medium

(B) Ion-exchange in neutral medium

Figure 21. Molecular interactions between a basic solute and the stationary phase. (A) Hydrogen-bonding (dipole-dipole) interaction between undissociated surface silanols and unprotonated amine solute. (B) Electrostatic interaction between ionized surface silanols and protonated amine solute leading to the reversible exchange or hydronium ion.

Figure 22. The effect of surface chemistry on the relative retention of aniline, N,N-DEA and norephedrine (related to phenol) with unbuffered mobile phases (see Table 4 for column ID).

Figure 23. Theoretical curves for the fraction of protonated species for selected base probes as a function of pH.

Figure 24 shows the relative retention of caffeine with respect to phenol, $\alpha_{C/P}$, (i.e., $k'_{\text{caffeine}}/k'_{\text{phenol}}$) in six different columns at pH 2 and 7. The hydride and to a lesser extent, the new ethyl adamantyl phase, exhibit the highest retention at both pH conditions. The values (less than one) indicate that caffeine eluted before phenol in all columns except the two mentioned above. The results at low pH conditions indicate that there is very little hydrogen bonding on all phases. The relatively high retention of the new adamantyl-ethyl phase can be associated with the lower surface coverage of the organic group.

Figures 25 through 30 show relative retention data, i.e., $\alpha_{B/P}$ ($k'_{\text{base}} / k'_{\text{phenol}}$) with respect to phenol for six different columns using several bases. As expected, all solutes, except amitriptyline, eluted before or co-eluted with phenol, indicating negligible contribution from hydrogen bonding. Figure 25 shows that 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 retention of aniline appears to be independent of the surface chemistry. Figures 26 and 27 show the retention behavior of bases with moderate pKa values, i.e., N,N-DMA and N,N-DEA. Except for a larger magnitude, the “bar group profiles” are quite parallel, with the conventional C₁₈ showing the greatest ion-exchange interactions. No significant advantage (i.e., enhanced shielding) appears to be provided by the adamantyl-containing bonded phases. The strong retention of N,N-DEA, as evidenced by high $\alpha_{B/P}$ values, agrees with similar findings by our research group [3] as well as others [4, 5, 6].

Figure 24. The effect of surface chemistry on the relative retention of *caffeine* with respect to phenol at two different pH values (see Table 4 for column ID).

Figure 25. The effect of surface chemistry on the relative retention of *aniline* with respect to phenol at two different pH values (see Table 4 for column ID).

Figure 26. The effect of surface chemistry on the relative retention of *N,N*-DMA with respect to phenol at two different pH values (see Table 4 for column ID).

Figure 27. The effect of surface chemistry on the relative retention of *N,N*-DEA with respect to phenol at two different pH values (see Table 4 for column ID).

Figure 28. The effect of surface chemistry on the relative retention of *norephedrine* with respect to phenol at two different pH values (see Table 4 for column ID).

Figure 29. The effect of surface chemistry on the relative retention of *ephedrine* with respect to phenol at two different pH values (see Table 4 for column ID).

Figure 30. The effect of surface chemistry on the relative retention of *amitriptyline* with respect to phenol at two different pH values (see Table 4 for column ID).

However, when compared with other phases, the hydride showed relatively strong hydrogen-bonding interactions and relatively weak ion-exchange interactions with these solutes. When basic solutes with high pKa values (i.e., > 9) are considered (specifically norephedrine and ephedrine as shown in Figures 28 and 29), it is the new C₁₈ that shows the strongest ion-exchange interactions with these solutes. The hydride also exhibits this behavior. Similarly, with N,N-DMA and N,N-DEA, no significant shielding appeared to be furnished by the bulky adamantyl groups. Except for the new C₁₈ phase, all bonded materials provided similarly efficient shielding toward silanolphilic interaction with basic solutes when amitriptyline was injected, and all columns showed adsorption of this compound at neutral pH ($k' > 30$ minutes).

None of the adamantyl containing groups appeared to furnish effective shielding under the conditions used. In other words, the structural rigidities of the ball-like adamantyl molecules did not show any superior properties of shielding compared to the linear C₁₈ phases.

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 10% of the peak height as depicted in Figure 31. Figures 32 to 38 comparatively show this parameter for several basic solutes eluted at pH 2 and 7. The column information along with the types of bonded phase and the preparation methods are listed in Table 4. A characteristic of these data is that the new C₁₈ phase shows a consistently larger asymmetry compared to those of all other phases.

On the other hand, the hydride phase (i.e., the one with the minimal shielding) shows very symmetric peaks, even for the high pKa solutes. More importantly, no significant improvement of peak symmetry can be associated with the adamantyl containing phases as compared to the C₁₈ phases.

It should be noted that our findings contradict with those of Gilpin et al. [2] and agree with those of Aubel et al.[21]. In Gilpin's work, only low pH conditions were used for high pKa solutes. Under these conditions, regular C₁₈ phases as well as static adamantyl containing ones behave similarly. Under these conditions, the silanols are completely protonated and no ion-exchange interactions exist. Additionally, strong hydrogen-bonding interactions at low pH conditions are more closely associated with the retention of the silica support (particularly its metal content) than to the type of bonding used [18]. The "real" test for silanophilic interactions is at neutral pH conditions where all silanols are ionized and can interact with cationic solutes.

Figure 31. Calculation of peak asymmetry by measuring the A/B ratio at 10% of the peak height.

Figure 32. The effect of surface chemistry on the relative asymmetry of *caffeine* with respect to phenol at two different pH values (see Table 4 for column ID).

Figure 33. The effect of surface chemistry on the relative asymmetry of *aniline* with respect to phenol at two different pH values (see Table 4 for column ID).

Figure 34. The effect of surface chemistry on the relative asymmetry of *N,N*-DMA with respect to phenol at two different pH values (see Table 4 for column ID).

Figure 35. The effect of surface chemistry on the relative asymmetry of *N,N*-DEA with respect to phenol at two different pH values (see Table 4 for column ID).

Figure 36. The effect of surface chemistry on the relative asymmetry of *norephedrine* with respect to phenol at two different pH values (see Table 4 for column ID).

Figure 37. The effect of surface chemistry on the relative asymmetry of *ephedrine* with respect to phenol at two different pH values (see Table 4 for column ID).

Figure 38. The effect of surface chemistry on the relative asymmetry of *amtriptyline* with respect to phenol at two different pH values (see Table 4 for column ID).

4. CONCLUSIONS

The fundamental objectives of the present work have been accomplished. We have demonstrated that adamantyl containing hydrocarboneous/phases can be readily prepared by catalytic hydrosilylation of vinyl-modified adamantanes on a hydride substrate. As expected, the reversed-phase HPLC behavior of the new phases appeared to be similar to that of “regular” C₁₈ phases. When basic solutes were used as test probes, the bulky ball-like adamantyl groups did not seem to be able to effectively shield 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 in a monomeric C₁₈ phase.

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