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New alumina-based stationary phases for high-performance liquid chromatography

Synthesis by olefin hydrosilation on a silicon hydride-modified alumina intermediate

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ABSTRACT

A silanization procedure is used to form a layer of silicon hydride on the surface of alumina. IR and NMR data confirm the presence of the hydride on the surface. Modification of the hydride intermediate is accomplished by reaction with a terminal olefin in the presence of a transition metal catalyst to form an alkyl-bonded material. Both IR and NMR confirm the bonding of the alkyl ligand to the hydride surface. Chromatographic tests indicate reversed-phase behavior. Exposure to high concentrations of phosphate solution for an extended period resulted in no significant deterioration of the bonded phase.

INTRODUCTION

Silica-based stationary phases for HPLC have dominated HPLC applications for three decades. Their main advantages include availability in a variety of particle and pore sizes, high mechanical strength and reproducible separations with the same column under controlled experimental conditions. However, there are some disadvantages which preclude silica from being a universal support for HPLC and/or limit the scope and type of separations possible. For example, there are many manufacturers of silica, each using its own process for production, which has resulted in a wide substrate variation. In addition, even from a single source there are significant batch to batch variations which often make comparisons between different columns of the same stationary phase difficult. Probably the most serious drawback of silica and derivatized silica involve its limited pH stability, generally in the range of 2 to 8 [1,2]. This has led to the development of novel modification schemes for silica [3], the incorporation of other compounds such as zirconia into the silica matrix [4], or the use of alternate materials such as polymers [5–7].

Alumina offers still another alternative to silica because of its inherent higher pH stability. However, in contrast to its extensive use as a medium in column chromatography for purification purposes or for separations in the normal-phase mode, there are still relatively few reports involving alumina-based materials in the reversed-phase (RP) mode. Considering that RP methods represent the majority of HPLC applications, it will be necessary to develop modified aluminas similar to those that exist for silica. Only then will it be possible to identify any advantages that alumina may possess over silica because of its fundamentally higher pH stability.

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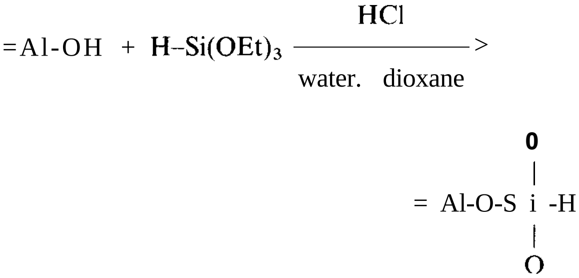
Knox and Pryde [8] were among the first to describe modifications to alumina which could be used in RP-HPLC. These phases were synthesized using standard organosilane chemistry which can be described by the following reaction:

$$=\text{Al-OH} + \text{X-Si(R}')_2(\text{R}'') \rightarrow\ =\text{Al–O–Si(R}')_2(\text{R}'') + \text{HX}$$

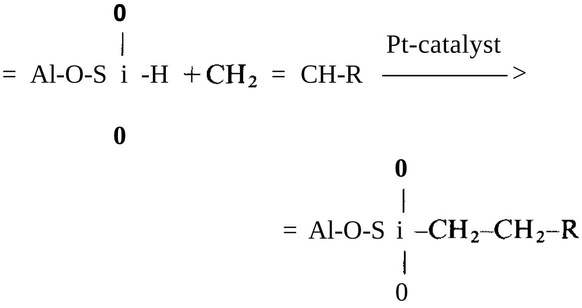
R' is generally a methyl group for typical monomeric and methoxy or ethoxy for polymeric stationary phases. However, no further work followed these initial reports. Another possibility involves physically coating alumina with a polystyrene–divinylbenzene copolymer, polybutadiene or polyoctadecylsilane [9]. These materials have excellent pH stability but often display strong retention, high column backpressures due to swelling in certain solvents and/or poorer chromatographic efficiency when compared to normal chemically bonded stationary phases [9]. Another approach for monomeric bonding can be accomplished by reacting organic phosphonic acids with alumina. This method leads to an = Al-O-P-R linkage at the surface. An octadecyl phase prepared by this approach was used in basic solvents (at pH values > 10) and with basic solutes [10]. However, no stability studies were done in order to determine the long-term reproducibility of these results. It was also noted that these linkages were unstable in phosphate buffer solutions. In another study, a variety of modification schemes involving Grignard reagents as well as organolithium and organoaluminum compounds were evaluated [11]. The results were not totally satisfactory but they certainly indicated that other methods of modification should be explored.

Recently it has been demonstrated that hydride intermediates on silica are a viable alternative to organosilane chemistry for producing bonded phases [12–14]. The final material contains a silicon-carbon bond at the surface which has been shown to have superior hydrolytic stability in comparison to the silicon-oxygen-siliconcarbon linkage that results when an organosilane reagent is used. The method involves forming a monolayer of silicon hydride on the surface which can then be reacted with a terminal olefin compound in the presence of a suitable catalyst to yield the final product. On silica, the hydride can be formed from either chlorination of the surface followed by reduction with a species such as lithium aluminum hydride [12] or by reacting silica with triethoxysilane (TES) in an acidic medium [15]. Since the latter procedure is both faster and more efficient, it is the method of choice for producing the hydride intermediate. A similar approach for the synthesis of monomeric alumina-based stationary phases is reported here. The silicon hydride-modified alumina is prepared by silanization with TES in the presence of water, HCl as a catalyst and dioxane as the solvent:



$$=\text{Al-OH} + \text{H–Si(OEt)}_3 \xrightarrow[\text{water. dioxane}]{\text{HCl}}\ =\text{Al-O-}\overset{\overset{\text{0}}{|}}{\underset{\underset{\text{O}}{|}}{\text{Si}}}\text{-H}$$

Bonding of the organic moiety then follows by hydrosilation of a terminal olefin on the hydride intermediate in the presence of a platinum catalyst:



$$=\text{Al-O-}\overset{\overset{\text{0}}{|}}{\underset{\text{0}}{\text{Si}}}\text{-H} + \text{CH}_2 = \text{CH-R} \xrightarrow{\text{Pt-catalyst}}\ =\text{Al-O-}\overset{\overset{\text{0}}{|}}{\underset{\underset{\text{0}}{|}}{\text{Si}}}\text{–CH}_2\text{–CH}_2\text{–R}$$

From a practical point, the above method does involve a two-step process in contrast to the single silanization reaction utilized in the preparation of commercial chromatographic materials. Therefore, reproducibility in the synthetic process will be an ultimate concern when considering the usefulness of the proposed method. This first report presents the synthetic protocol for the proposed method as well as spectroscopic and preliminary chromatographic evaluation of the new material. Subsequent reports will give involve more rigorous chromatographic testing.

EXPERIMENTAL

Materials

Alumina (Biotage) with a mean particle size of 8 pm, a mean pore size of 334 Å and a BET surface area of 49.0 m^2/g was dried overnight at 110°C under vacuum before use. In the synthethic procedures, TES (Huls America), 1-octene and 1-octadecene (Sigma) were used as received. The solutes used in the chromatographic testing were purchased (Aldrich) in the highest purity available. Water was purified on a Millipore filter system. All other mobile phases were of HPLC quality and synthetic materials were purchased in reagent grade. A commercial sample of C_{18} phosphonate alumina (Biotage) was used for comparison studies.

Synthetic procedures

Preparation of silanized alumina. Dried alumina (5 g) was placed in a 250-ml three-neck round-bottom flask with 110 ml of dioxane. The flask was placed in an oil bath at 80°C and then 5 ml of 3.1 A4 HCl was added while stirring. After several min 35 ml of TES (0.2 *M* in dry dioxane) in a self-equalizing funnel was added dropwise. This corresponds to a 10% excess of TES with respect to hydroxides on the alumina surface as determined by thermogravimetric analysis (TGA). The mixture was then refluxed for 5 h to ensure complete reaction of the available hydroxide groups [15]. After this period the TES alumina was washed successively twice with 100-ml portions of dioxane-water (80:20), dioxane and ether. The solid was then dried at room temperature for 4 h at atmospheric pressure followed by 1 h at 110°C under vacuum.

Preparation of C_8 and C_{18} alumina. The olefin (150 ml) and 1 .OO ml of 50 m*M* dicyclopentadienyl platinum (II) in dry chloroform were placed in a three-neck round-bottom flask equipped with a condenser and a magnetic stirrer. The mixture was heated up to 70°C and maintained at this temperature until the solution became clear (at least 1 h). Then 5.0 g of hydride alumina (predried overnight) was added slowly by means of an addition funnel. After all the hydride alumina was in the flask, the solution temperature was raised to 85°C and maintained at this temperature for 96 h. The product was washed consecutively with 100-ml portions of toluene (4 times), dichloromethane (2 times) and diethyl ether (2 times). The final product was first dried in air at room temperature for 12 h and then under vacuum at 110°C for 12 h.

Product evaluation and characterization

Spectroscopic and elemental analysis. All samples were analyzed by diffuse reflectance infrared Fourier transform (DRIFT) on a Perkin-Elmer Model 1800 spectrometer. Elemental analysis was performed on a Perkin-Elmer Model 240C Elemental Analyzer. TGA was done on a Perkin-Elmer Model 2 instrument. Differential scanning calorimetric (DSC) was done on a Perkin-Elmer Model 7 system. ^{13}C, ^{29}Si and ^{27}Al cross-polarization magic-angle spinning (CP-MAS) NMR spectra were obtained on a Bruker MSL 300 spectrometer. For ^{13}C and ^{29}Si, parameters similar to those reported in the literature were used [16]. For ^{27}Al, a recycle time of 5 s and a contact time of 5 ms required about 2000 scans to obtain the typical spectrum. Spectral simulation was done using the LINESIM program provided with the instrument. Analysis of silicon by atomic spectroscopy was done on a Beckman SMI Model III d.c. plasma spectrometer.

Stability studies. A methanol-water (0.1 *M* pH 7 phosphate buffer) (50:50) was used as the mobile phase. A test mixture (theophyline, p-nitroaniline, methylbenzoate, phenetol and o-xylene) was injected after each 100 column volumes of mobile phase.

Chromatographic studies. The bonded aluminas were packed into a 150 × 4.6 mm I.D. stainless-steel column using a pneumatic amplification pump (Haskel) with methanol as the driving solvent. The instrumentation consisted of a Hewlett-Packard Model 1050 HPLC equipped with quaternary solvent delivery, an autosampler, a variable wavelength detector and a Chemstation for data analysis.

RESULTS AND DISCUSSION

In order for efficient silanization to occur on the alumina surface, it is necessary to know reasonably well the number of hydroxides per unit area. This can be determined by TGA analysis which gives a value of about 40 $\mu mol/m^2$. This value is certainly high when compared to most common chromatographic silicas which have about 8 $\mu mol/m^2$. However, it has been shown [15] that certain silicas (Vydac TP, The Separations Group) sometimes give values in excess of 40 μmol/m^2 for hydroxide determination by TGA and this has been attributed to either a large number of micropores and/or some tightly held water that is not easily removed during the initial heating to 110°C although the latter is unlikely under the drying condition used [17]. Since it is not known whether all hydroxyls measured by TGA will react during the silanization process, the nominal 10% excess of reagent used in the reaction may actually represent a considerably greater value.

The success of the silanization process can most easily be evaluated by DRIFT analysis. Fig. 1A is the spectrum of bare alumina which can be compared to Fig. 1B of the hydride-modified alumina showing the strong Si-H stretching band near 2260 cm-‘. However, the position and width of the band are constant even as the extent of silanization is varied. The total amount of silane on the surface is determined by placing the material in strong base (0.1 A4 NaOH), heating and stirring for several h in order to strip off the silicon layer(s). Analysis by plasma emission spectroscopy results in a value of 15.1 μmol/m^2 of Si on the surface. Only 38% of the total hydroxides as determined by TGA apparently reacted. Therefore, the unreacted OH groups probably represent hydroxides which are inaccessible to the TES because of steric considerations [17].

A much better indication concerning the nature of the hydride-modified material can be obtained

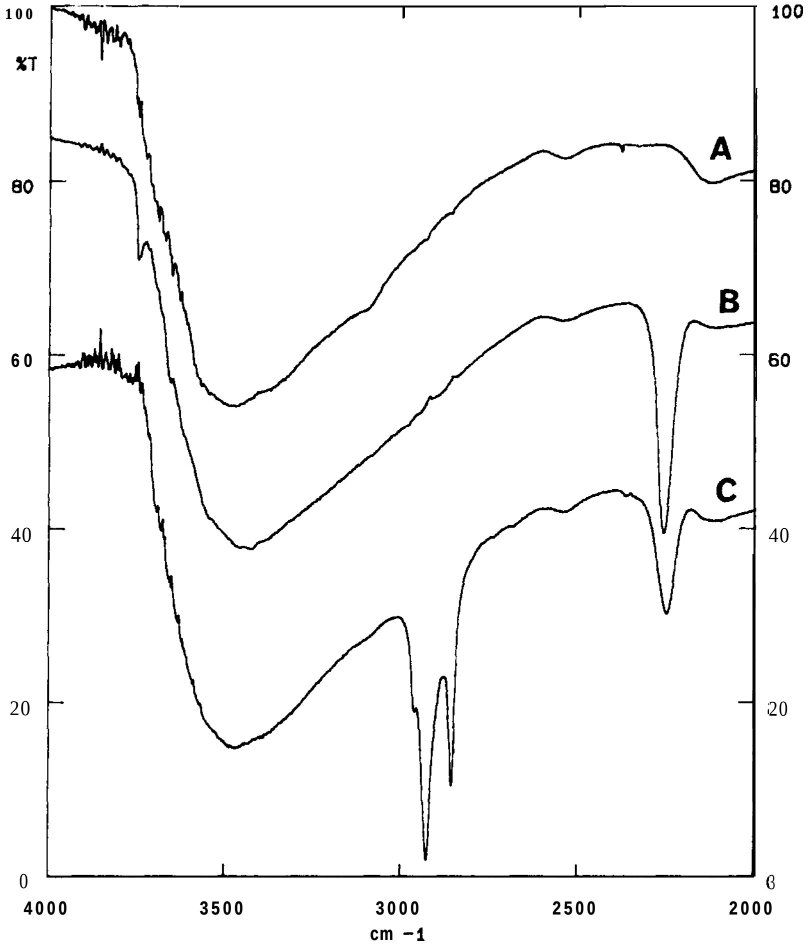


Fig. 1. DRIFT spectra of alumina materials: (A) bare alumina, (B) hydride alumina and (C) reaction product of hydride alumina with I-octadecene.

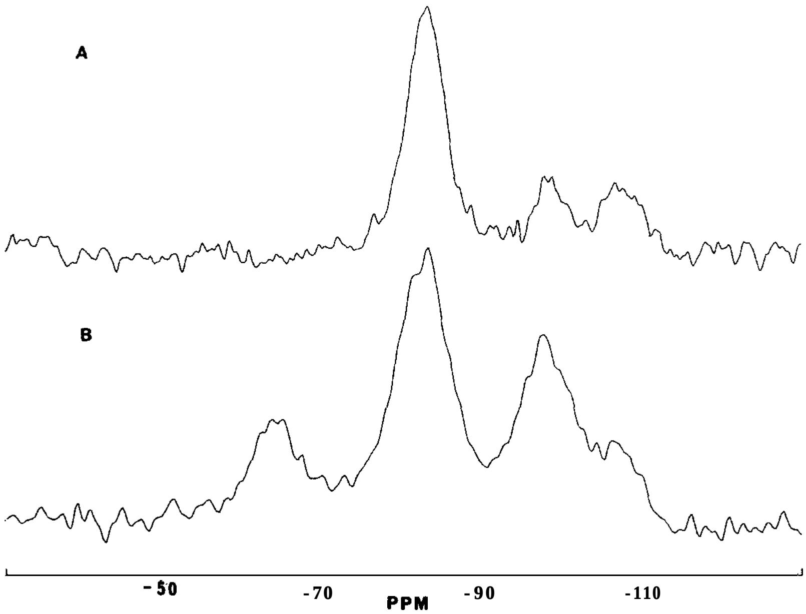


Fig. 2. ^{29}Si CP-MAS-NMR spectra of alumina materials: (A) hydride alumina and (B) reaction product of hydride alumina with 1-octadecene.

from the ^{29}Si CP-MAS-NMR spectrum. Fig. 2A shows a typical spectrum of an alumina following reaction with TES. The major peak at -85 ppm can be readily assigned to the Si-H group. However, two other minor peaks are also present in the spectrum. By analogy to spectra taken on silica, the peak at -110 ppm (Q_4) can be assigned to a silicon with four siloxane bonds while the peak at -100 ppm (Q_3) can be assigned to a silicon that has three siloxane bonds and one hydroxide group. These resonances are not part of any expected monolayer or multilayer structure since each silicon atom must have a hydride attached to it. Therefore the presence of Q_4 and Q_3 resonances must be due to either impurities in the starting reagent or some subsequent decomposition of the hydride-modified surface. Additional experiments are currently underway to study this problem. Despite these unknown aspects of the hydride surface, it was decided to try the olefin additions and test the product phases.

Both 1-octene and 1-octadecene were catalytically bonded to the hydride-modified material. Elemental analysis of the two products gave coverages of 5.5 and 4.4 μmol/m^2 for the C_8 and C_{18} bonded phases, respectively. This represents reaction of 36% and 29% of the available hydrides for the two materials. Fig. 1C is a typical infrared spectrum of a product phase from the reaction of 1-octadecene with the hydride alumina. The strong bands between 2800 and 3000 cm^{-1} are the expected C-H stretching vibrations for the bonded alkyl moiety. The appearance of the C-H bands is accompanied by a diminishing of the Si-H band at 2260 cm-‘, which is expected when the hydride reacts with the olefin.

The success of the bonding reaction can also be confirmed by CP-MAS-NMR spectroscopy. Fig. 2B shows the ^{29}Si spectrum of the C_{18} bonded phase. In comparison to the hydride material, an additional peak at about -65 ppm is observed which can be attributed to the Si-C linkage formed in the bonding process. As expected a decrease in the signal intensity of the Si-H peak near -85 ppm occurs. The presence of the siloxane species (Q_4 and Q_3), as evidenced by the peaks at -110 and -100 ppm, are even more prominent in this spectrum. It is unclear whether there is an actual increase in intensity of these peaks, or as is more likely, their relative intensity compared to the other peaks in the spectrum has increased. When compared to the

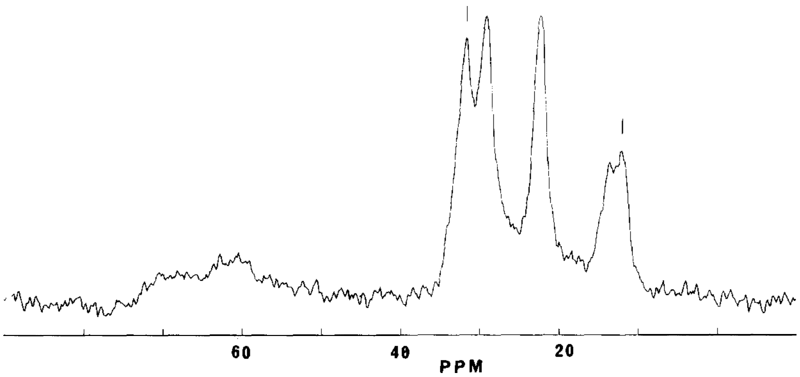


Fig. 3. ^{13}C CP-MAS-NMR spectrum of product from the reaction of hydride alumina with I-octene

spectrum of hydride material, the Q_3 peak has apparently increased relative to the Q_4 peak. Fig. 3 shows the ^{13}C CP-MAS spectrum of the octyl material which also verifies the bonding of the alkyl via olefinic addition. The peak positions in this spectrum as well as that of the C_{18} are identical to those obtained for bonding similar species to silica surfaces [16].

Finally, the ^{27}Al CP-MAS-NMR spectrum provides additional evidence to characterize the modification of the surface. Fig. 4A is the ^{27}Al spectrum of the C_{18} modified alumina. Similar to other reports in the literature on aluminas [18,19], the spectrum consists of two major peaks: the smaller peak at about 60 ppm represents tetrahedrally (T_d) coordinated aluminum ions and the peak at 1 ppm represents octahedrally (O_h) coordinated aluminum ions. The T_d resonance is about 18% of the total peak area which is in good agreement with the 15–20% tetrahedrally coordinated Al^{3+} found in most hydrated aluminas. Fig. 4B is the simulated spectrum while Fig. 4C represents the individual components in the simulated spectrum. Whether the three peaks in the simulated O_h portion of the spectrum are due to three different Al^{3+} environments or whether this just represents an increased distortion of octahedral symmetry by modification that results in enhanced quadrupolar effects (for ^{27}Al, $I = 5/2$) due to a non-symmetric electric field gradient is not clear. However, in the absence of effective cross-polarization (CP) the distortion in the octahedral peaks is much less indicating that species being observed in the CP spectrum are close to the surface where all of the available hydrogens are located. Table I is a comparison of the various peak areas for the bare, hydride, C_{18} and commercial aluminas. The areas of peaks 1 (T_d) and 2 remain relatively constant within experimental error except for the C_{18} sample which appears to decrease slightly while peak 3 decreases. Peak 4 is not present for the bare alumina, is small for the hydride alumina species and increases further for the C_{18} alumina. The appearance of peak 4 can be interpreted as the formation of new species (hydride or alkyl bonded moiety) or by an increased distortion of the O_h symmetry during the modification process.

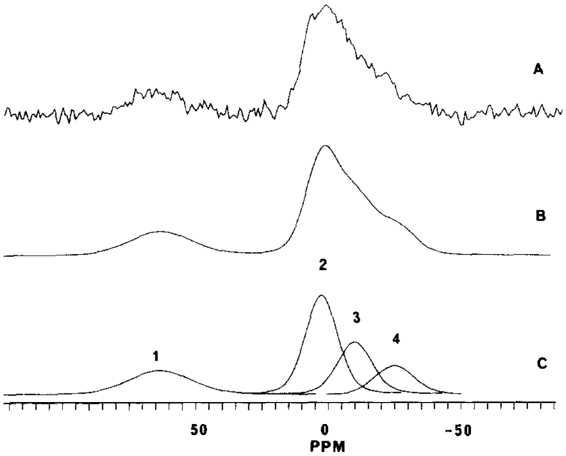


Fig. 4. ^{27}Al CP-MAS-NMR spectra of product from the reaction of hydride alumina with 1-octadecene: (A) experimental spectrum, (B) simulated spectrum and (C) simulated spectrum with individual components.

TABLE I

RELATIVE PEAK AREAS FOR SIMULATED COMPONENTS IN ^{27}Al CP-MAS-NMR SPECTRA OF VARIOUS ALUMINAS

Sample	Peak numbef			
	T_d	O_h		
	1	2	3	4
Bare alumina	0.18	0.48	0.33	-
Hydride alumina	0.16	0.52	0.28	0.05
C_{18}alumina	0.20	0.43	0.24	0.14
Biotage C_{18} (phosphonate ester)	0.17	0.51	0.24	0.08

[a] Refer to Fig. 4 for peak labeling. Error in relative peak areas, ± 0.03.

Fig. 5 shows the DSC/air curve of the hydride modified alumina. There is a single distinct peak for the thermooxidative process which has a maximum between 520–530°C. This can be compared to similar peaks for the polyhydrosiloxane (polymerization product of TES in the absence of alumina) which occurs at 365°C and the peak for hydride silica which occurs at 430–450°C [15]. Two conclusions can be drawn from this result. First, it is clear from the large shift in the peak for the thermooxidative process that the hydride surface is chemically bonded to the alumina surface as opposed to being a physically adsorbed layer of polymerized material. Second, the shift to an even higher temperature for alumina when compared to silica indicates a greater thermal stability for the hydride-modified silica. This may be useful when comparing the relative chemical stabilities under agressive mobile phase conditions.

Since the spectroscopic studies indicated both successful formation of a hydride surface and subsequent hydrosilation with an olefin, some preliminary chromatographic experiments were undertaken in order to determine the retention properties of these materials. A test mixture consisting of theophylline, p-nitroaniline, methylbenzoate, phenetol and o-xylene was run on both the C_{18} alumina synthesized from the hydride intermediate and a commercial C_{18} alumina. The chromatograms are shown in Fig. 6A and B, respectively. In general separation is good by both materials with slightly more asymmetry, except for theophylline, in the peaks for the phosphonate column. Table II sum-

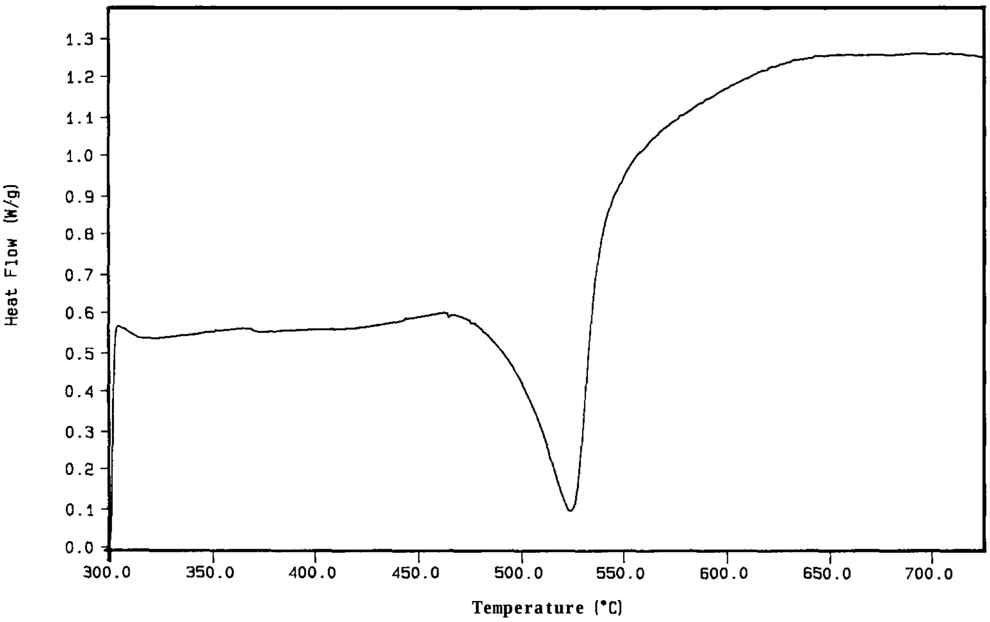


Fig. 5. DSC curve for the thermooxidation of hydride-modified alumina.

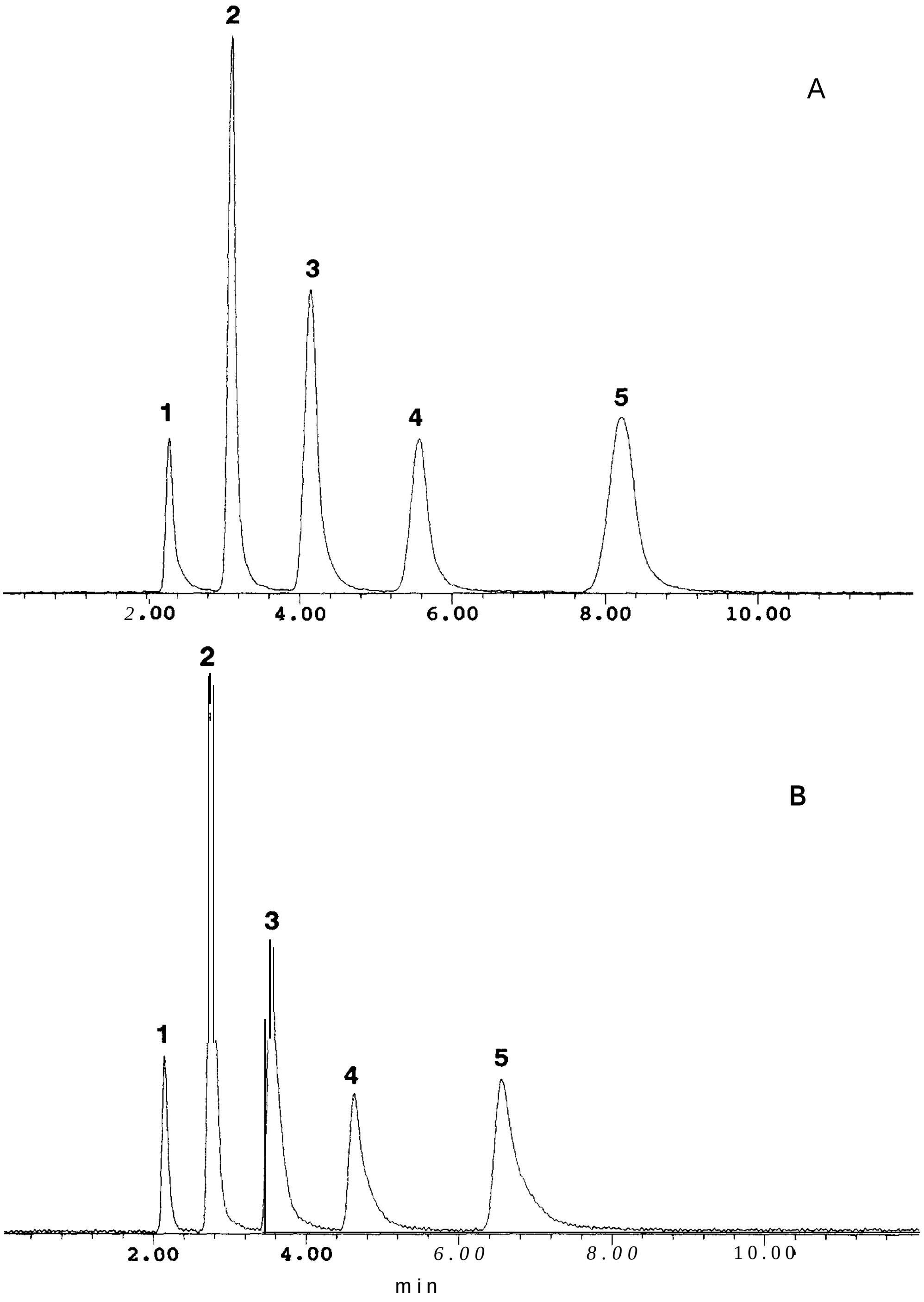


Fig. 6. Chromatogram of test mixture for reversed-phase behavior: (A) C_{18} from hydride and (B) phosphonate C_{18}. Mobile phase: acetonitrile-water (50:50). Peaks: 1 = theophylline; 2 = p-nitroaniline; 3 = methylbenzoate; 4 = phenetol: 5 = o-xylene.

TABLE II

EFFICIENCIES AND PEAK SYMMETRIES FOR HYDROSILATION AND PHOSPHONATE ALUMINA C_{18} COLUMNS

Peak[a]	Efficiency	Assymmetry factor
Hydrosilation C_{18} column		
1	860	2.15
2	3070	1.40
3	1500	1.60
4	1930	1.35
5	2000	1.25
Phosphonate C_{18} Column		
1	1880	2.10
2	1890	2.50
3	1150	2.70
4	1030	2.85
5	950	3.10

[a] Refer to Fig. 6 for peak identification.

marizes the efficiency (calculated with a base at 10% of the peak height) for both types of columns. Data for the C_8 column from the hydride intermediate gave similar results to the C_{18} but with lower capacity factors. Both the C_8 and C_{18} phases synthesized in this study were exposed to phosphate containing mobile phases at neutral pH with no evidence of deterioration in chromatographic performance or loss of bonded material as measured by elemental analysis.

In conclusion, it appears that the silanization/olefin addition procedure is a viable approach to the synthesis of various alkyl-bonded stationary phases on alumina. The product shows no evidence of decomposition in the presence of phosphate, as is reported for the commerical material. Preliminary chromagraphic results indicate satisfactory separation under reversed-phase conditions where peak symmetry is good. Future studies will involve the nature of the hydride layer and its effect on chromatographic properties as well as the stability of the bonded material under more severe mobile phase conditions.

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