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(54) **MICROMACHINED GAS CHROMATOGRAPHY COLUMNS FOR FAST SEPARATION OF ORGANOPHOSPHONATE AND ORGANOSULFUR COMPOUNDS AND METHODS FOR DEACTIVATING SAME**

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(57) **ABSTRACT**

Improved microcolumns and methods for producing microcolumns particularly suitable for use in gas chromatographs are disclosed. In particular, following deposition of the stationary phase coating, the microcolumns are subjected to a postcoating treatment with a molecule that binds to the active sites in the stationary phase column thereby eliminating or reducing loss of gas chromatograph performance associated with those active sites. The postcoating treatment molecule binds to the same active sites as the analytes of interest.

18 Claims, 11 Drawing Sheets

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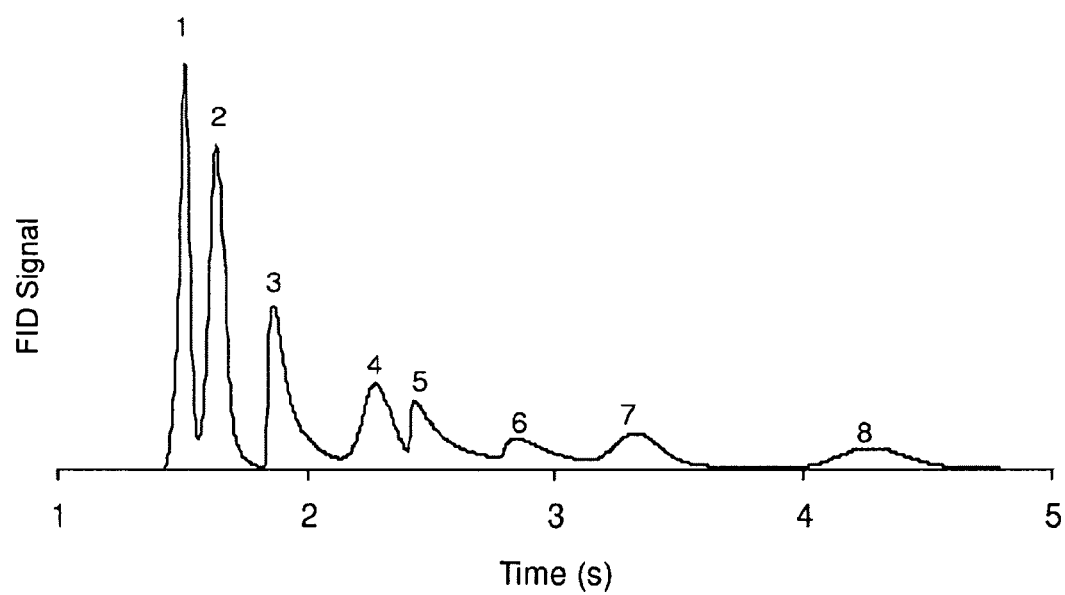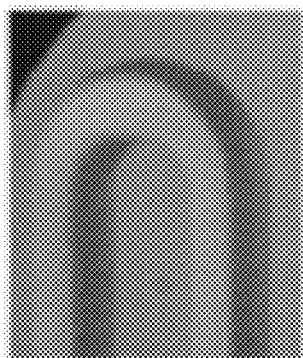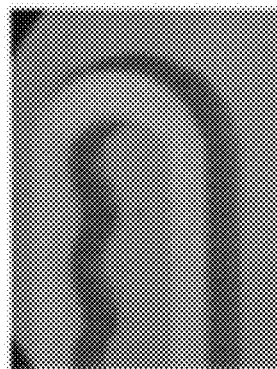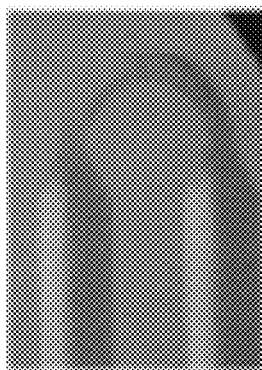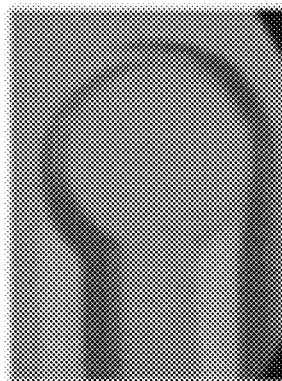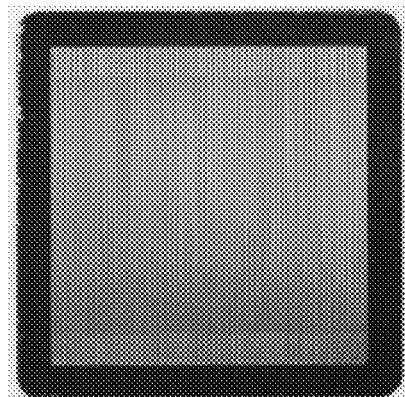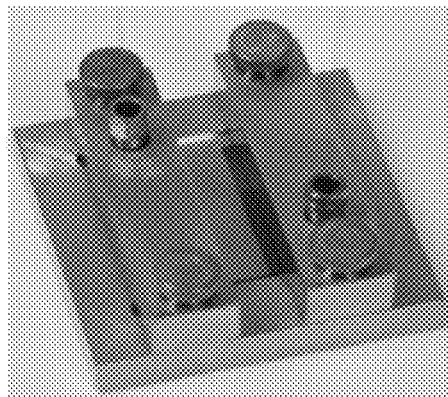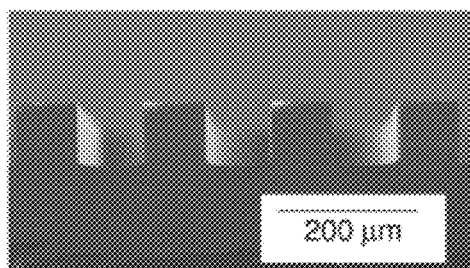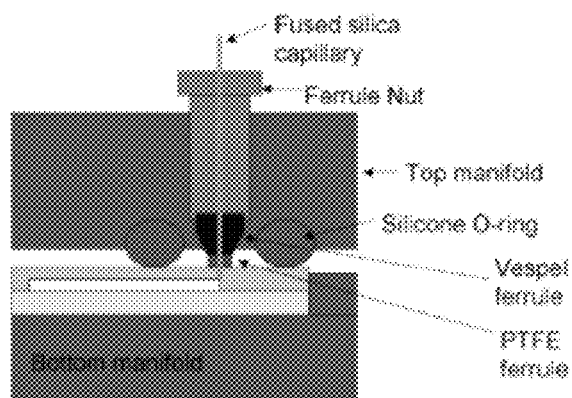
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FIGURE 1

Panel A

Panel B

Panel C

Panel D

FIGURE 2

Panel A

Panel C

Panel B

200 μm

Panel D

Fused silica
capillary

Ferrule Nut

Top manifold

Silicone O-ring

Vespel
ferrule

PTFE
ferrule
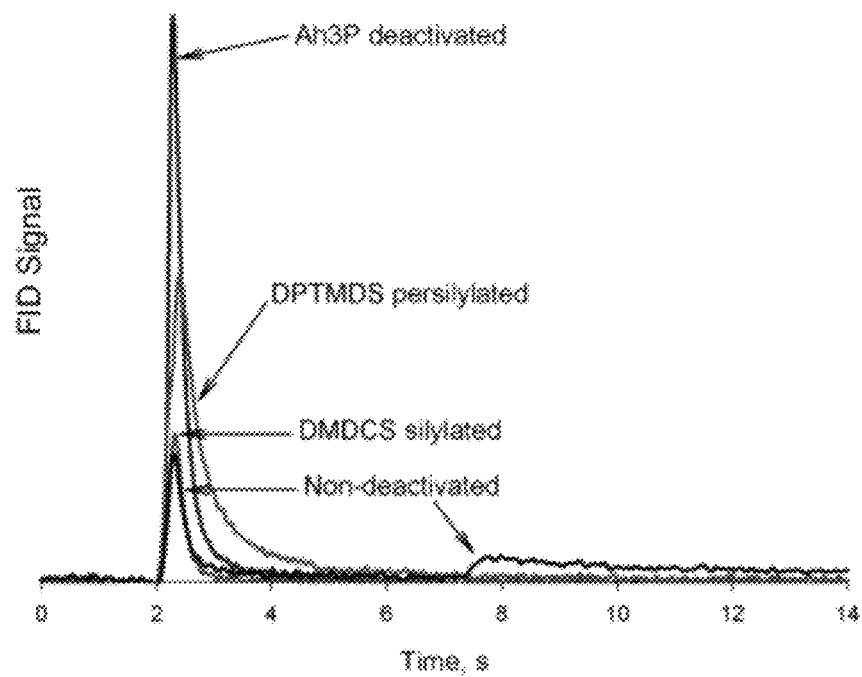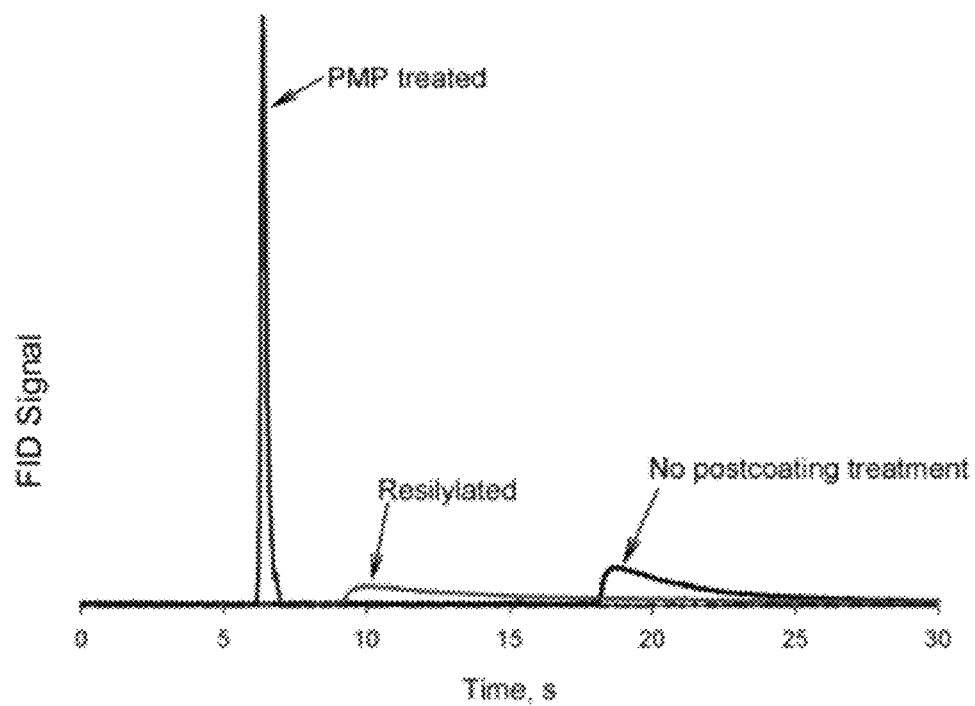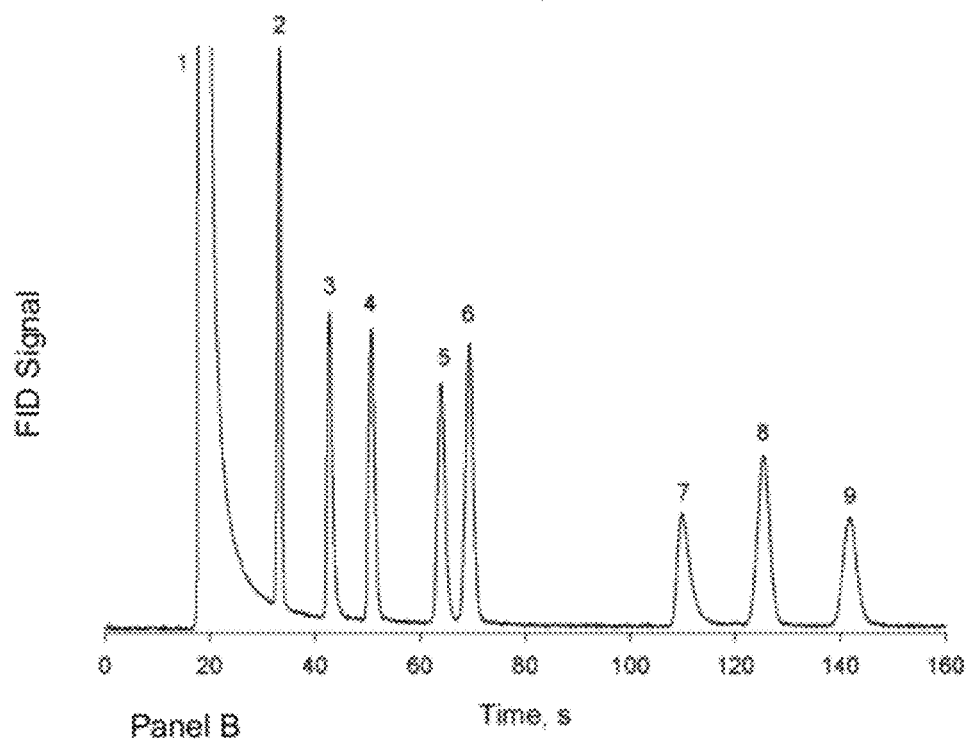
FIGURE 3

Panel A

Panel B

FIGURE 4

FIGURE 5

FIGURE 6

FIGURE 7

FIGURE 8

FIGURE 9

Panel A

Panel B

FIGURE 10

Panel A

Panel B

FIGURE 11

1

MICROMACHINED GAS CHROMATOGRAPHY COLUMNS FOR FAST SEPARATION OF ORGANOPHOSPHONATE AND ORGANOSULFUR COMPOUNDS AND METHODS FOR DEACTIVATING SAME

CROSS-REFERENCES TO RELATED APPLICATIONS

This application claims priority to and benefit under 35 U.S.C. §119(e) to U.S. Provisional Application Ser. Nos. 61/021,588 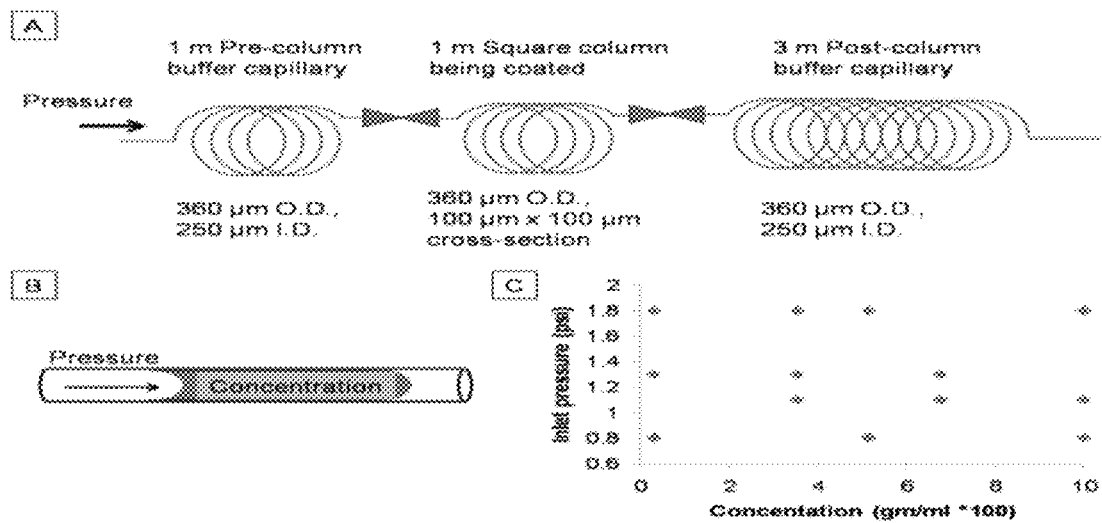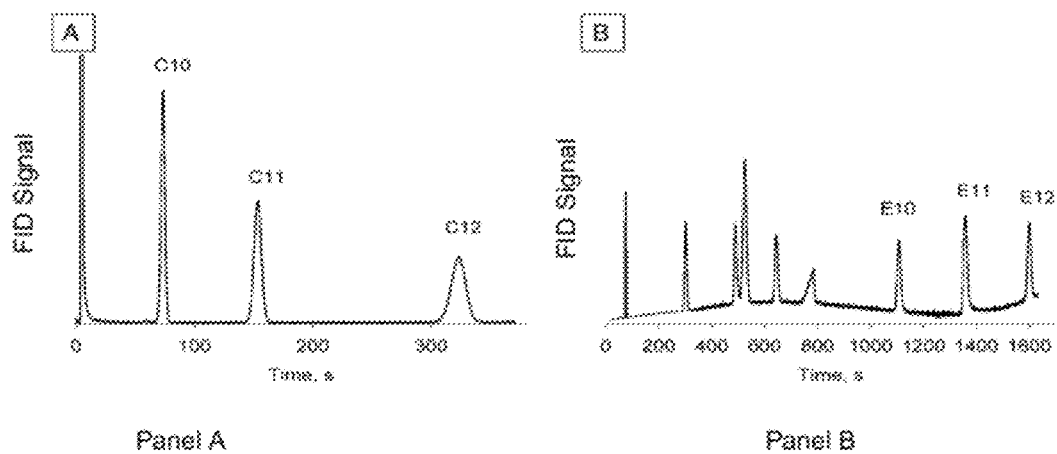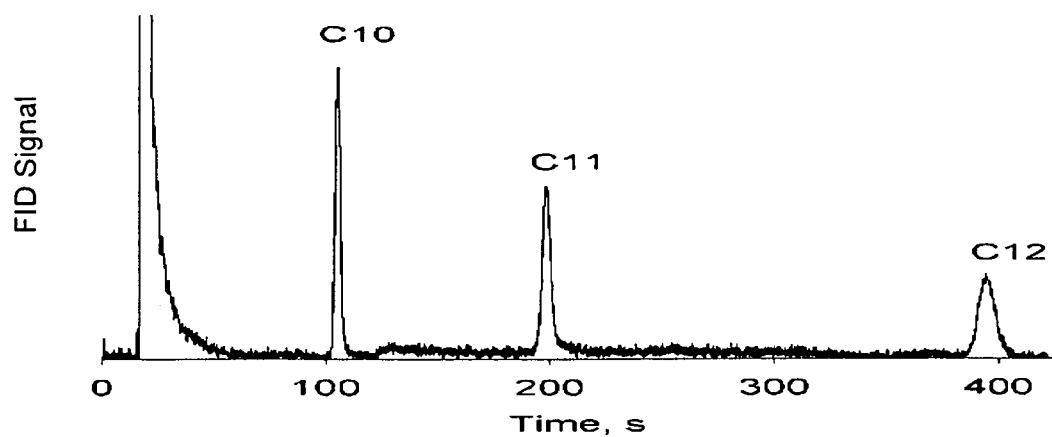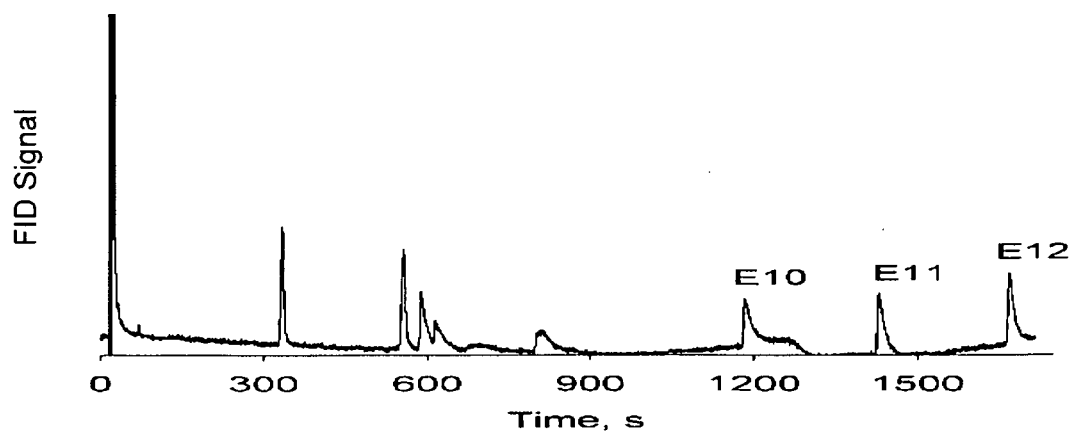and 61/021,620, both filed Jan. 16, 2008, the disclosures of which are herein incorporated by reference in their entirety herein.

STATEMENT AS TO RIGHTS TO INVENTIONS MADE UNDER FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

This invention was made, at least in part, with U.S. government support under the Defense Advanced Research Projects Agency (DARPA) under U.S. Air Force Grant FA8650-04-1-7121. The Government has certain rights in this invention.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The invention relates generally to columns and methods for producing microcolumns suitable for use in gas chromatographs. In particular, following deposition of the stationary phase coating, the microcolumns are subjected to a postcoating treatment with a molecule that binds to the active sites in the stationary phase column thereby reducing or eliminating loss of gas chromatograph performance associated with those active sites.

2. Related Art

A gas chromatograph (GC) is a chemical analysis instrument used for separating chemicals in a complex sample and is generally composed of three basic parts, an injector, a column, and a detector. Different chemical constituents of a sample pass in a gas stream through the column at different rates depending on their various chemical and physical properties and their interaction with a specific column filling, called the stationary phase. As the chemicals exit the end of the column, they are detected and identified electronically. Conventional GC columns are generally small open tubes with internal diameters in the range of about 270 microns to about 530 microns and lengths in the range of about 10 meters to 30 meters. The inside walls of these columns are coated with a thin even layer of organic polymer, the GC liquid phase, to a thickness of less than about one micron.

Microfabricated gas chromatograph (µGC) column development has received considerable interest for the analysis of toxic chemicals, explosives, disease markers and other analytes. In general, column fabrication starts with first etching microfluidic channels in a silicon or glass wafer and then sealing the etched microfluidic channels using anodic or fusion bonding. The microcolumn walls are then deactivated. Subsequently, static or dynamic coating techniques may be used to deposit the stationary phase inside the microcolumn prior to analyte analysis.

Many studies have reported columns that can separate hydrocarbons and a few studies have reported microfabricated columns that are able to show significant separation of organophosphonates. In the organophosphonate separation studies, however, the organophosphonate peaks exhibit sig-

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nificant tailing due to unwanted adsorption to the active sites present in the microcolumn. FIG. **1** shows a fast µGC chromatogram, however, most noteworthy is that the dimethyl methyl phosphonate (DMMP), diethyl methyl phosphonate (DEMP), and diisopropyl methyl phosphonate (DIMP) peaks tail, which makes the microcolumns less than optimal for fast portable GC. Accordingly, there is a need for improved deactivation of the walls of columns, particularly in microcolumns suitable for use in GCs and µGCs.
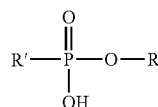
BRIEF SUMMARY OF THE INVENTION

The invention provides improved microcolumns and methods for producing microcolumns having enhanced GC performance. In one aspect, following deposition of the stationary phase, the microcolumns are subjected to post-treatment with a molecule that binds to the active sites in the stationary phase, thereby reducing or eliminating loss of GC performance associated with those active sites.

According to one aspect of the invention, a method for preparing a gas chromatograph (GC) column may include deactivating a plurality of walls of a GC column, depositing a stationary phase in the GC column, and treating the GC column with a molecule such that the molecule binds to active sites in the stationary phase of the column.
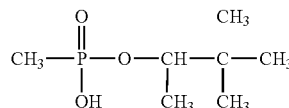
The deactivating step may employ a method such as silylation, perisilylation, and deactivation using an organosilicon hydride, for example. Specifically, the silylation may be performed using DMDCS, the perisilylation may be performed using Ah3P, and the deactivation with the organosilicon hydride may be performed using DPTMDS.

The postcoating molecule may be an acid including hydrocarbon ligands, a base including hydrocarbon ligands, a thiol, a phosphine, and/or an amine. Moreover, the postcoating molecule may be a structure of Formula I:

Formula 1

$$R' - \overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle OH}{|}}{P}} - O - R$$

where r and r' are linear branched or substituted hydrocarbons. More specifically, the postcoating molecule may be the structure of Formula II:

Formula 2

$$CH_3 - \overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle OH}{|}}{P}} - O - \overset{\overset{\displaystyle}{\underset{\underset{\displaystyle CH_3}{|}}{CH}} - \overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}} - CH_3$$

In another aspect according to the invention, a gas chromatograph (GC) column prepared by the methodology of the invention may include deactivating a plurality of walls of a GC column, depositing a stationary phase in the GC column, and treating the GC column with a molecule such that the molecule binds to active sites in the stationary phase of the column. The stationary phase may be applied at a pressure of about 0.9 psi and at a concentration of about 10 w/v %.

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The GC column may include a postcoating molecule having a structure of Formula III:

Formula 1

$$R' - \overset{\displaystyle O}{\underset{\displaystyle OH}{\overset{\|}{P}}} - O - R$$

where R and R' are linear branched or substituted hydrocarbons. Specifically, the GC column may include a molecule having the structure of Formula II:
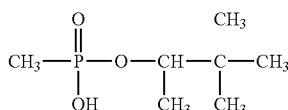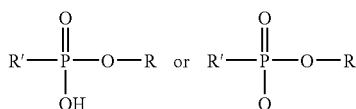
Formula 2

$$CH_3 - \overset{\displaystyle O}{\underset{\displaystyle OH}{\overset{\|}{P}}} - O - CH - \overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}} - CH_3$$

The GC column may include a postcoating molecule having the structure of Formula III:

Formula 3

$$R' - \overset{\displaystyle O}{\underset{\displaystyle OH}{\overset{\|}{P}}} - O - R \quad or \quad R' - \overset{\displaystyle O}{\underset{\displaystyle O}{\overset{\|}{P}}} - O - R$$
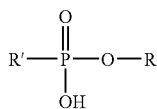
where R and R' are linear branched or substituted hydrocarbons.

According to one aspect of the invention, a GC column may include a plurality of column walls each having a deactivated inner surface, a stationary phase layer deposited on the deactivated inner surface of the column walls, a plurality of binding sites in the stationary phase layer, and a post-coating molecule bound to at least one of the binding sites in the stationary phase layer. The inner surface of the column walls may be deactivated with a compound selected from the group consisting of DMDCS, Ah3P, and DPTMDS. The stationary phase layer may have a thickness of about 0.1 μm and may be uniformly spread over the inner surface of said plurality of column walls. The column walls may have a serpentine configuration. The column walls may be rounded.
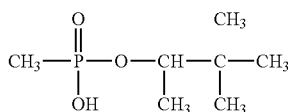
The post-coating molecule may have a structure of Formula I:

Formula 1

$$R' - \overset{\displaystyle O}{\underset{\displaystyle OH}{\overset{\|}{P}}} - O - R$$

where R and R' are linear branched or substituted hydrocarbons.

The post-coating molecule may have the structure of Formula II:

Formula 2

$$CH_3 - \overset{\displaystyle O}{\underset{\displaystyle OH}{\overset{\|}{P}}} - O - CH - \overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}} - CH_3$$

4

The post-coating molecule may have the structure of Formula III:

$$R' - \overset{\displaystyle O}{\underset{\displaystyle OH}{\overset{\|}{P}}} - O - R \quad or \quad R' - \overset{\displaystyle O}{\underset{\displaystyle O}{\overset{\|}{P}}} - O - R$$
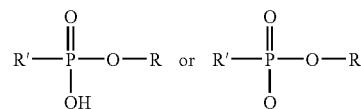
where R and R' are linear branched or substituted hydrocarbons.

The post-coating molecule may be one or more compounds such as a thiol, a phosphine, and an amine.

Additional features, advantages, and embodiments of the invention may be set forth or apparent from consideration of the following detailed description, and claims. Moreover, it is to be understood that both the foregoing summary of the invention and the following detailed description are exemplary and intended to provide further explanation without limiting the scope of the invention as claimed.

BRIEF DESCRIPTION OF THE DRAWINGS

The accompanying drawings, which are included to provide a further understanding of the invention, are incorporated in and constitute a part of this specification, illustrate embodiments of the invention and together with the detailed description serve to explain the principles of the invention. No attempt is made to show structural details of the invention in more detail than may be necessary for a fundamental understanding of the invention and various ways in which it may be practiced.

FIG. 1 is a chromatogram showing a 4 second separation obtained in the conventional OV-5 coated microcolumn. The separation was obtained by 1 μl headspace injection with a split of 100:1, column inlet pressure held at 25 psi and oven temperature ramped from 90° C. to 98° C. at 12° C./min. Hydrogen was used as the carrier gas. Peaks represent (1) ethyl ether, (2) Toluene, (3) dimethyl methyl phosphonate, (4) diethyl methyl phosphonate, (5) n-octanol, (6) diisopropyl methyl phosphonate, (7) 1,6-dichlorohexane, and (8) dodecane. Notable is that the dimethyl methyl phosphonates, diethyl methyl phosphonate, octanol and diisopropyl methyl phosphonates peaks tail, leading to an apparent non-zero baseline between 2 and 3.3 seconds.

FIG. 2: are photographs showing bend geometries that may be used for constructing the analytical columns according to principles of the invention. Panel A is a photograph showing circular bends. Panel B is a photograph showing sine wave bends. Panel C is a photograph showing conically converging bends. Panel D is a photograph showing concentrically converging bends.

FIG. 3: Panel A is a photograph showing a 3 meter long micromachined serpentine column on a 3.2 cm square and 500 μm thick silicon piece anodically bonded to 1 mm thick Pyrex 7740®, constructed according to principles of the invention. Capillaries were attached to the back of the column using an in-house made manifold as indicated in FIG. 1D. Restek (#560292) deactivated guard columns (I.D. 200 μm, O.D. 100 μm) were used to make all connections. Panel B is a scanning electron micrograph of 100 μm wide and 100 μm deep channels, constructed according to principles of the invention. Panel C is a photograph of brass manifold packaging for a microcolumn produced by principles of the invention. Panel D is a schematic showing details of a low dead volume connection to the microcolumn constructed according to principles of the invention.

FIG. 4 shows two chromatographs. Panel A is a chromatograph comparing diisopropyl methyl phosphonate injections on a non-coated nondeactivated silicon microcolumn, a persilylated microcolumn constructed according to principles of the invention, a DMDCS silyated microcolumn constructed according to principles of the invention, and a Ah3P treated microcolumn constructed according to principles of the invention. Panel B is a chromatograph comparing n-octanol injections on a non-coated nondeactivated silicon microcolumn, a persilylated microcolumn constructed according to principles of the invention, a DMDCS silyated microcolumn constructed according to principles of the invention, and a Ah3P treated microcolumn constructed according to principles of the invention. 5 μl headspace of sample was injected on 35 cm long microcolumns with a split of 50:1 and oven temperature and inlet pressure held at 75° C. and 5 psi respectively. Hydrogen was used as the carrier gas.

FIG. 5 is a chromatograph comparing injections for diisopropyl methyl phosphonate headspace injection on a Ah3P deactivated and a OV-5 coated microcolumn without further treatment, and with further heat treatment with re-silylating agent (Rejuv-8®) according to principles of the invention and with pinacolyl methylphosphonate according to principles of the invention. The analysis was carried out on coated 3 meter long microcolumns by injecting 5 μl headspace with a split of 50:1 and oven temperature and inlet pressure held at 120° C. and 10 psi respectively. Hydrogen was used as the carrier gas.

FIG. 6 is a chromatograph showing the separation of phosphonate and sulfur compounds described in Table 2 on the pinacolyl methyl phosphonate treated microcolumn of the invention. Testing was carried out using hydrogen as carrier gas. 1 μl headspace of the mix was injected with a split of 120:1, the oven temperature held at 110° C. and inlet pressure ramped from 35 psi to 45 psi at the rate of 150 psi/min.

FIG. 7 shows two chromatographs of column test mix injections. Panel A is a chromatograph of column test mix injections on Ah3P deactivated and OV-5 coated without PMP treatment. Panel B is a chromatograph of column test mix injections on Ah3P and OV-5 coated with PMP treatment according to principles of the invention. 1 μl of test mix liquid was injected with a split of 1000:1, column temperature held at 120° C. and inlet pressure adjusted to achieve a helium carrier gas velocity of 20 cm/s.

FIG. 8 is a Fourier transform infrared spectrum of a PMP treated OV-5 microcolumn constructed according to principles of the invention.

FIG. 9 is a schematic showing the column arrangement during the dynamic coating of a 1 m long square capillary column (Panel A), variables altered in coating the column (Panel B), and the design of experiment implemented.

FIG. 10 shows two chromatograms showing separation of n-C_{10} to n-C_{11} alkanes (Panel A) and Grob's mix (Panel B) on square capillary column coated with parameters (0.9 psi pressure and 10 w/v % concentration) that would allow creating square column with best performance as indicated by the model optimization.

FIG. 11 shows two chromatograms showing separation of n-C_{10} to n-C_{11} alkanes (Panel A) and Grob's mix (Panel B) on square capillary column coated with parameters (2.7 psi pressure and 10 w/v % concentration) that would allow creating square column with better performances as indicated by the model optimization.

DETAILED DESCRIPTION OF THE INVENTION

It is understood that the invention is not limited to the particular methodology, protocols, and reagents, etc.,

described herein, as these may vary as the skilled artisan will recognize. It is also to be understood that the terminology used herein is used for the purpose of describing particular embodiments only, and is not intended to limit the scope of the invention. It also is noted that as used herein and in the appended claims, the singular forms "a," "an," and "the" include the plural reference unless the context clearly dictates otherwise. Thus, for example, a reference to "a bend" is a reference to one or more bends and equivalents thereof known to those skilled in the art.

Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which the invention pertains. The embodiments of the invention and the various features and advantageous details thereof are explained more fully with reference to the non-limiting embodiments and examples that are described and/or illustrated in the accompanying drawings and detailed in the following description. It should be noted that the features illustrated in the drawings are not necessarily drawn to scale, and features of one embodiment may be employed with other embodiments as the skilled artisan would recognize, even if not explicitly stated herein. Descriptions of well-known components and processing techniques may be omitted so as to not unnecessarily obscure the embodiments of the invention. The examples used herein are intended merely to facilitate an understanding of ways in which the invention may be practiced and to further enable those of skill in the art to practice the embodiments of the invention. Accordingly, the examples and embodiments herein should not be construed as limiting the scope of the invention, which is defined solely by the appended claims and applicable law. Moreover, it is noted that like reference numerals reference similar parts throughout the several views of the drawings.

Accordingly, provided immediately below is a "Definition" section, where certain terms related to the invention are defined specifically for clarity, but all of the definitions are consistent with how a skilled artisan would understand these terms. Particular methods, devices, and materials are described, although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the invention. All references referred to herein are incorporated by reference herein in their entirety.

DEFINITIONS

Ah3P is Phenyltris(dimethylsiloxy)silane
BOE is Buffered Oxide Etching
DMDCS is Dimethyldichlorosilane
DEMP is Dimethyl Methyl Phosphonate
DIMP is Diisopropyl Methyl Phosphonate
DMMP is Dimethyl Methyl Phosphonate
DPTMDS is Diphenyltetramethyl Disilazane
DRIE is Deep Reactive Ion Etching
FTIR is Fourier Transform Infrared Spectroscopy
GC is Gas Chromatograph
HF is Hydrofluric Acid
HMDS is Hexamethyldisilazane
KOH is Potassium Hydroxide
μGC is Microfabricated Gas Chromatograph
OP is Organophosphonate
OS is Organosulfur
OV-5 is 5% diphenyl 95% dimethylpolysiloxane
PMP is Pinacolymethyl Phosphonate
SiO_2 is Silicon Dioxide
The invention relates generally to columns and methods for preparing columns for use in μGCs and also conventional

GCs, which result in sharp µGC or GC peaks on chromatographs, with relatively little or no peak tailing characteristics. In particular, the microcolumns of the invention following stationary phase coating may be subjected to a post-coating treatment with a molecule that strongly binds to the active sites in the stationary phase column thereby "deactivating" the active sites associated with the stationary phase and reducing or eliminating the loss of µGC performance or GC performance associated with those active sites. The molecule should bind strongly to the same active sites as the analytes of interest and may be or the same or heavier molecular weight. The molecule, however, has to be fairly volatile so it does not contaminate the stationary phase. Specifically, for example, the microcolumn may be postcoated with an alkylating phosphonate. The alkylating phosphonate functions by deactivating sites in the stationary phase that cause phosphonate peaks to tail "permanently."

According to one embodiment of the invention, the microcolumns of the invention may be produced by employing the following fabrication sequence: (i) etching microfluidic channels in a substrate; (ii) employing anodic or fusion bonding to seal the etched microfluidic channels to create microcolumns; (iii) deactivating the microcolumn walls; (iv) depositing the stationary phase within the microcolumns by employing static or dynamic coating; and (v) post-treating with a molecule that binds with the active sites within the stationary phase.

The microfluidic channels of the invention may be fabricated by etching the surface by employing deep reactive ion etching (DRIE), Bosch, or other etching processes appropriate for forming the desired microfluidic channel structure in the material of the substrate or the wafer. Other suitable fabrication techniques known by those of skill in the art may include mechanical machining or laser milling, embossing or molding of polymeric compositions, photo-lithography of UV-curable polymer compositions, and photoforming layers. In a particular aspect, the columns may be constructed using advantageous channel architectures, such as a serpentine channel structure, spiral channel structure, or rectangular channel structure. Moreover, the serpentine channel structure may be constructed to exhibit various bend geometries for enhancing µGC separation, as disclosed in U.S. Appln. No. 61/021,588. The geometric bends may include circular bends (FIG. 2, Panel A), sine wave bends (FIG. 2, Panel B), conically converging bends (FIG. 2, Panel C), and concentrically converging bends (FIG. 2, Panel D), for example. Substrates or wafers that may be employed in the invention may be any suitable material such as silicon, glass, polyimide, silicon carbide, nickel, and other materials that are easy to fabricate. For example, etching and sealing of the microfluidic channels may be accomplished by the exemplary procedures described in Preparatory Example 1, below. FIG. 3 shows images of a microfabricated column of the invention prepared by the procedures described in Preparatory Example 1. FIG. 3 shows a microcolumn having a series of 100 microns wide, 100 microns deep channels on a 3.2×3.2 cm silicon wafer arranged in a serpentine pattern.

The microcolumns of the invention may have a diameter in the range of about 20 microns to about 1000 microns, and specifically in a range of about 25 microns to 250 microns, and more specifically in the range of about 25 microns to about 50 microns. The columns may have a depth in the range of about 20 microns to about 600 microns, and specifically in the range of about 50 to about 250 microns. The microcolumns may have a length in the range of about 0.3 meters to about 50 meters, and in particular, a length of about 1 to 10 meters. The spacing between adjacent channels may be less

than about 4 times the microcolumn channel diameter, and specifically may be in the range of about 30 microns to about 200 microns In one particularly advantageous embodiment of the invention, the microcolumns may be about 3 meters long, about 100 microns wide, about 100 microns in depth, and have about 100 micron spacing between channels.

The etching process used to fabricate the channels structures of the invention, however, may undesirably generate scallops, indentations, or rough edges in the walls of the channels. The rough edges may be undesirable because they may interfere with attaining an uniform stationary phase deposition and ultimately effect the resolution of the GC by causing band broadening. Therefore, according to a further aspects of the invention, the methodology may further include smoothening the channel walls by employing a buffered ion etching (BOE) or an anodization process as disclosed in U.S. Appln. No. 61/021,588.

As appreciated by those of skill in the art, BOE, also known as buffered HF or BHF, is a wet etchant used in microfabrication. Its primary use is in etching thin films of SiO_2 or silicon nitride (Si_3N_4). In general, BOE comprises a mixture of a buffering agent, such as ammonium fluoride (NH_4F), and HF. A common BOE solution may comprise a 6:1 volume of about 40% NH_4F in water to about 49% HF in water, which will etch thermally grown oxide at approximately 2 nm/s at 25° C. BOE is used to remove SiO_2 and is a very selective etch because it stops etching at the silicon and does not etch any further. In a specific aspect, a substantially even wet oxide layer having a thickness of about 2 mm may be grown on the DRIE channel walls in silicon and may be subsequently smoothened by BOE to remove the wet oxide completely.

In another embodiment, the DRIE channel walls may be smoothened by employing anodization. Anodization is a standard electrochemical technique known by those skilled in the art for making porous silicon and involves the application of a potential to a bulk silicon sample or silicon wafer. The silicon wafer may be immersed in an electrolyte solution which is commonly a mixture of HF, water and other components. The silicon wafer is held positive and a platinum mesh is used a negative electrode. In one specific aspect, porous silicon may be grown using anodization and subsequently etched using a mild potassium hydroxide (KOH) solution. The silicon anodization may take place at $0.25 A/cm^2$ in a 1:1 HF and ethanol electrolytic bath. Typical mild KOH concentrations may include molar solutions in the range of about 5 molar to about 10 molar.

In another embodiment, the DRIE channels may be rounded by dynamically coating a glass layer. In this process, a glass deposition solution (e.g., spin on glass from Filmtronics (P120F and 550F, for example) or Honeywell (512B, for example)) is used to coat channel surface. Thicker later of glass may be deposited in the corners, which avoids pooling of stationary phase in the subsequent process of coating a stationary phase.

In a further embodiment, the rounded micro-columns may be created by using buried structure channels (BSC). BSC may be created by etching the channels first with a DRIE, followed by a wall protection with silicon dioxide and the last step of iso-etching with SF6 RIE. This process results in partially buried micro-columns with minimum corners and hence even deposition of stationary phase when coating them.

In one embodiment of the invention, the channel walls may be smoother than about one order of magnitude less than the phase thickness. For example, if the phase thickness is about 400 nm, then the channel walls should have a smoothness of about 40 nm or if the phase thickness is 100 nm, then the channel walls should have a smoothness of about 10 nm.

Moreover, the etching process may also create undesirable sharp bends in the channel structure, which may cause the stationary phase to build up in the corners of the bends and negatively effect the resolution of the μGC. Therefore, if desired, the radius of the bend may be reduced by rounding off the bottom of the bend in the channel structure to promote uniform phase coating as disclosed in U.S. Appln. No. 61/021,588.

According to one embodiment, the radius of the corner of the bend may be at least about 10 times larger than the phase thickness, thus with about a 400 nm phase thickness, the corners should have a radius of greater than about 4 microns. The corners of the bends may be rounded off chemically using the anodization procedure described above, by machining or molding, or by coating with a suitable polymer or glass.

In one embodiment of the invention, the etched microchannels may be sealed by anodic or fusion bonding. In anodic bonding, the silicon and Pyrex© 7740 glass pieces are cleaned using RCA1 clean process, brought in surface contact, heated to 450-500° C., and applied a bias of 800-1200V. In fusion bonding the two cleaned silicon surfaces are brought in contact and heated in a furnace tube at 1100° C. Micromachined columns are commonly made of trenches in silicon. The surface of silicon is usually p or n doped, and therefore the surface may be doped with impurities and terminated with hydroxyl groups. The micromachines columns are usually sealed with Pyrex®. The Pyrex® may be engineered to form an anodic bond with silicon and match the coefficient of thermal expansion with silicon. Anodic bonding may be performed at about 1000 V and in a range of about 400° C. to about 500° C. The anodic bonding mechanism explains the flow of metal positive ions especially sodium when high electric field is applied during bonding process. The high temperature reduces the resistance to ion diffusion within Pyrex®. Therefore, such microcolumns may contain high ion contents near the Pyrex© surface as compared to silicon or conventional fused silica columns.

According to another embodiment of the invention, the sealed microcolumn walls may be deactivated prior to deposition of the stationary phase. Deactivation of fused silica columns is very well studied. Since fused silica itself is an inert material, it requires less surface modification thereby allowing stationary phase deposition. The microcolumn may be deactivated by utilizing silylation using DMDCS, perilsilyation using Ah3P, and/or deactivation with an organosilicon hydride such as DPTMDS, for example. Exemplary deactivation procedures using silyation, perilsilyation, and organosilicon hydride deactivation is described in Preparatory Example 2, below.

FIG. 4 (Panels A and B) shows how three different deactivation procedures of the invention silylation, persilylation, and Ah3P treatment affect the DIMP (FIG. 4, panel A) and n-octanol (FIG. 4, Panel B) peaks. As shown in FIG. 4, Panel A, the DIMP injection on non-deactivated microcolumn resulted in two peaks, a small sharper peak at 2.4 seconds and a heavily tailing peak at 7.8 seconds. DIMP injection on microcolumns silylated with DMDCS resulted in only one slightly sharper peak at 2.4 seconds (FIG. 4, Panel A). DIMP injection on microcolumns perilyated with DPTMDS resulted in one big peak at 2.7 seconds (FIG. 4, Panel A). This DIMP peak, however, has a half peak width of 0.9 seconds and a strong tailing characteristic (FIG. 4, Panel A). The DIMP injections on the microcolumn deactivated with Ah3P resulted in a sharp peak at 2.4 seconds with a peak width of 0.4 seconds, with little or no tailing characteristic (FIG. 4, Panel A).

The presence of the two peaks in the non-deactivated microcolumn may be due to the saturation and desaturation of reversible phosphonate binding sites. Sample loss occurs via irreversible binding of the phosphonates. Activity test results for deactivated microcolumns showed improvement over non-deactivated microcolumns. DMDCS silylation eliminated the reversible phosphonate binding sites and only showed one DIMP peak. DPTMDS persilylation produced better response and hence better deactivation to DIMP injection compared to DMDCS silanization treatment. This occurred because persilylation produces a denser film over the surface than silylation, and thereby lower gas permeability towards the surface of the microcolumn. For DPTMDS and Ah3P deactivations, Ah3P deactivation blocked the reversible and irreversible phosphonate binding sites more efficiently and produced better deactivation than DPTMDS, and accordingly, the Ah3P deactivated microcolumn had a better response to DIMP injection than the DPTMDS deactivated microcolumn.

As shown in FIG. 4, Panel B, n-octanol injection on a non-deactivated microcolumn resulted in a peak at 2.4 seconds with strong tailing characteristics. No additional peaks were observed with n-octanol injections as were with the DIMP injections shown in FIG. 4, Panel A, described above. The n-octanol injections on the DMDCS silylated microcolumn resulted in a peak at 2.45 seconds with a slightly higher peak height and a shoulder (FIG. 4, Panel B). This peak showed less tailing characteristics compared to the non-deactivated microcolumns. The n-octanol peak on the DPTMDS persilylated microcolumn resulted in a peak at 2.35 seconds and had a higher peak height and peak area compared to silylated and non-deactivated microcolumns (FIG. 4, Panel B). The n-octanol peak on the Ah3P deactivated microcolumn resulted in a peak at 2.4 seconds and showed the highest peak height amongst all the deactivations, with little or no tailing characteristics (FIG. 4, Panel B).

The n-octanol injections on the non-deactivated column exhibited heavy tailing and did not produce two peaks as with the DIMP injections. This indicated the presence of other active sites beside hydrogen binding sites, which actively adsorb phosphonates and do not adsorb n-octanol. The DMDCS silylated microcolumn produced a peak with slightly higher peak height and reduced peak tailing compared to peaks eluted from non-deactivated columns. The DPTMDS persilylated microcolumn and Ah3P deactivation produced higher levels of deactivation. As seen in FIG. 4, Panel B, the Ah3P deactivated microcolumn resolution was the best. The results shown in FIG. 4, Panels A and B, indicate that DIMP headspace injection was a very sensitive tracer for phosphonate binding sites in the microcolumn compared to n-octanol.

Accordingly, as shown in FIG. 4, Panel A and Panel B, Ah3P deactivation surprisingly renders the non-deactivated microcolumn surface more inert to organophosphonate and sulfur compounds, compared to persilylation and silylation methods of deactivation. Also, diisopropyl methyl phosphonate was found to be a better tracer for microcolumn activity towards organophosphonates compared to n-octanol.

According another embodiment, the inside surfaces of the microcolumns may be coated with a stationary phase material to enhance the separation of the chemical analytes of interest in the gas mixture to be analyzed. The stationary phase material may be a polymer having a specific chemical group with the proper physico-chemical interaction to cause separation of the analytes. Suitable stationary phase materials are generally known by those of skill and the art and may be purchased from Agilent (HP-1 ms, DB-1 ms, HP-1, DB-1, HP-5

ms, DB-5, HP-5, DB-5 ms, DB-1301, DB-35, HP-35, DB-35 ms, DB-1701, DB-1701P, for example) Alltech (AT-1 ms, At-1ht, At-20, At-FAME, At-CAM, At-Amino Acid, AT-Sulfur, for example), or Restek (Rtx/MXT-1, Rtx/MTX-1301, Rtx/MXT/XTI-5, for example). The microcolumns may be coated with the stationary phase material by a number of methods known by those skilled in the art. Methods may include, for example, filling the column with a solvent containing the stationary phase material and then applying a vacuum to the end of the column to dry the solvent out of the column, or by using sol-gel techniques, static techniques, or dynamic techniques. The thickness of the stationary phase may be about 0.1 μm, uniformly spread over the inner surface of the microcolumn with minimum or no pooling. Exemplary procedures for stationary phase coating are described in Preparatory Example 3, below.

According to another embodiment, the microcolumns may be post-treated after stationary phase deposition with a molecule that binds to the active sites in the stationary phase microcolumn. As described above, the molecule should bind to the same active sites as the analytes of interest, but should be substantially volatile so it does not contaminate the stationary phase. Additionally, the postcoating molecule may be of equal or greater molecular weight than the analyte of interest. Exemplary procedures for post-coating the microcolumn are described in Preparatory Example 4, below.
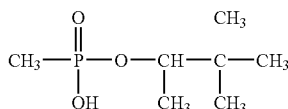
In one embodiment, if the analyte of interest is an organophosphonate (OP) or organosulfur (OS), the post-treatment molecule may have a structure of Formula I:

Formula 1

$$R'—\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle OH}{|}}{P}}—O—R$$
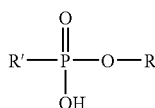
where R and R' are linear branched or substituted hydrocarbons that would also poison the base sites in the stationary phase. Commercially available compounds may include ethyl-methyl phosphonate (CAS 1832-53-7), cyclohexyl hydrogen methylphosphonate (CAS 1932-60-1) isopropyl methylphosphonic acid (CAS 1832-54-8) and pinacolyl methylphosphonate (PMP) (CAS 616-52-4), for example.

In a specific embodiment, pinacolyl methylphosphonate (PMP) (CAS 616-52-4) having a structure of Formula II, below, may be used to post-treat the microcolumn:

Formula 2

$$CH_3—\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle OH}{|}}{P}}—O—\overset{}{\underset{\underset{\displaystyle CH_3}{|}}{CH}}—\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}—CH_3$$

Depending upon the analyte of interest, additional post-treatment molecules may include OS, thiols for the Lewis base sites, and phosphines for acid sites, and amines for acid sites.

FIG. 5 shows effects of two post-coating treatments: resilylation and PMP treatment on Ah3P deactivated microcolumns. DIMP injections on a no-postcoating microcolumn resulted in a peak at 18.1 seconds and exhibited strong tailing characteristics. The Rejuv-8 (Sigma Aldrich, St. Louis, Mo.) resilylated microcolumn resulted in faster elution of the DIMP at 9.8 seconds. This DIMP peak was smaller in height

and exhibited stronger tailing characteristics compared to the no-postcoating treatment microcolumn. PMP treatment of the microcolumn decreased the retention time of DIMP peak to 6.7 seconds. This DIMP peak was much sharper, slightly asymmetric and showed little or no tailing characteristics. The peak width at half height of the DIMP peak was 0.15 seconds.

The effect of post-coating treatment on phosphonate activity was carried out on 3 meter long, OV-5 coated, Ah3P deactivated microcolumns. DMMP (Sigma Aldrich, Santa Clara, Calif.), DEMP (Sigma Aldrich, Santa Clara, Calif.), DIMP, TEP (Sigma Aldrich, Santa Clara, Calif.) were the organophosphonates and isopropyl sulfide (IPS) (Sigma Aldrich, Santa Clara, Calif.), chloroethyl methyl sulfide (CEES) (Sigma Aldrich, Santa Clara, Calif.), and isopropyl sulfonyl chloride (IPSC) (Fluka, Santa Clara, Calif.) were the organosulfur compounds used in this study. A mix comprising of reagents listed in Table 1, immediately below was prepared.

TABLE 1

No.	Compound
1	2-chloro-2-methylpropane
2	Ethyl ether
3	Isooctane
4	Diisopropyl sulfide
5	Chloroethyl methyl sulfide
6	Nonane
7	Dimethyl methyl phosphonate
8	Isopropane sulfonyl chloride
9	Decane
10	Diethyl methyl phosphonate
11	Diisopropyl methyl phosphonate
12	Undecane
13	Triethyl phosphate
14	Menthone
15	Isoborneal
16	Dodecane

FIG. 6 shows the separation of an OP and sulfur compound mix (described in Table 1, above) on a PMP postcoated, Ah3P deactivated microcolumn of the invention. The numbers in Table 1, above, correspond to the numbered peaks in FIG. 6. As shown in FIG. 6, the fast GC chromatogram shows easily resolvable and less tailing peaks of OP (peaks 7, 10, 11, 13) and OS compounds (peaks 4, 5, 8). Peak 10 corresponding to diethyl methylphosphonate (DEMP) shows an assymetric peak having some residual activity. The separation of compounds was obtained within a 4 seconds long window.

FIG. 7 (Panel A and Panel B) shows the microcolumn activity testing results obtained by injecting Agilent's DB-5 microbore column test mix (contents listed in Table 2, below). Panel A, is a chromatograph of test mix injections on an Ah3P deactivated, OV-5 coated, no-postcoated microcolumn, and Panel B is a chromatograph of test mix injections on an Ah3P deactivated, OV-5 coated, PMP postcoated microcolumn. The mix was formulated to detect the presence of different characteristic active sites in the microcolumn. The mix contains n-octanol and n-decanol for the detection of hydrogen binding sites such as silanol (Si—OH) groups. 2,6-dimethylphenol and 2,6-dimethylaniline were used for Lewis acidic and basic active site detection. The metal adsorptive sites were detected using napthalene. The methyl decanoate and alkanes were used for computing microcolumn efficiency and checking presence of dead volumes and microcolumn overloading.

TABLE 2

No.	Compound
1	Hexane
2	Decane
3	n-Octanol
4	2,6-dimethyl phenol
5	2,6-dimethyl aniline
6	Napthalene
7	n-Decanol
8	Tridecane
9	Methyl decanoate

The numbers in Table 2, above, correspond to the numbered peaks in FIG. **7**, Panels A and B. As shown in FIG. **7**, Panel A, test mix injection on the microcolumn showed strong adsorption of n-octanol, n-decanol and 2,6-dimethylaniline peaks. The n-octanol peak was present in tailing parts of peak **4**. This was confirmed using mass spectrometry. The n-decanol peak eluted as a shoulder to the baseline at 135 seconds on the chromatogram. The napthalene peak exhibit slight tailing characteristics. The number of theoretical plates were calculated based on the tridecane peak. The tridecane peak showed an adjusted retention time (t_R) of 1.773 minutes and a peak width of 0.034 minutes. Using equation (1) number of theoretical plates were calculated to be about 15000.

As shown in FIG. **7**, Panel B, test mix injection on the PMP treated microcolumn exhibited sharp peaks for n-octanol, n-decanol and 2,6-dimethylaniline elution. N-decanol exhibited slight tailing characteristics. The tridecane peak was eluted at an adjusted retention time of 1.802 minutes and had a peak width of 0.033 minutes. The number of theoretical plates on the PMP treated microcolumn were calculated to be about 16500.

Among the post-coating treatments, resilylation reduced the phosphonate retentive nature of the microcolumn, however the tailing behavior remained. Heat treatment with PMP showed reduction in DIMP peak tailing behavior and produced a sharp peak profile. Microcolumn test mix results showed that OV-5 coated microcolumn with Ah3P deactivation showed high adsorption activity for n-octanol, n-decanol and 2,6-dimethylaniline, indicating presence of hydrogen bonding sites and acidic sites or hydrogen bonding sites of acidic nature. PMP treatment caused suppression of microcolumn activity towards octanol, decanol and dimethylaniline by poisoning the active sites. Commercial microcolumn test mix injection showed a significant decrease in the microcolumn's hydrogen bonding sites of acidic nature with PMP treatment. The theoretical number of plates on a 3 meter microcolumn increases with PMP treatment by about 1500. This corresponds to an increase of about 3% in theoretical plate numbers on one meter basis. This may be due to swelling of the stationary phase or inconsistency in the dynamic coating process.

FIG. **8** is a FITR spectrum that was obtained by subtracting the FTIR results for PMP postcoated from no-postcoated OV-5 coated, Ah3P deactivated microcolumns. Strong phosphoryl stretching vibration (P=O) was evident at 1205 cm^{-1}. This indicated the presence of adsorbed phosphonates species on the surface. The spectrum region from 3000 cm^{-1} to 2800 cm^{-1} shows a typical fingerprint exhibited by CH$_3$O and CH$_3$P vibrations in the condensed-phase PMP spectrum. The spectrum shows presence of pinacolyl skeletal vibrations from 1240-1270 cm^{-1}.

Interpretation of the FITR spectra of compounds containing both P—OH and P—OR functionalities in alkyl hydrogen methylphosphonates was complicated by the fact that they

give rise to strong P—O— stretching vibrations, which was common to both groups. In the spectrum, P—O—C group presence produced a strong absorption band in the region of 1000 cm^{-1}. Unlike the liquid PMP spectrum showing three broad peaks around 1000 cm^{-1}, the spectrum in FIG. **8** shows only one absorption band. That fact combined with the absence of O—H stretching absorption peak in the region of 2525-2780 cm^{-1} implied that the final microcolumn comprised the species of the form in Formula 3

Formula 3

$$R' - \overset{\displaystyle O}{\underset{\displaystyle O}{\overset{\|}{\underset{\|}{P}}}} - O - R$$
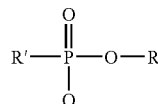
FTIR results indicated the presence of PMP after PMP heat treatment of coated microcolumns in vacuum. FTIR results in conjunction with GC analysis indicated that PMP chemisorbs at the active sites responsible for organophosphonate peak tailing. When the same amounts of liquid DMMP, DIMP, DEMP or TEP were injected, the subsequent organophosphonate headspace injections did produce sharp peaks. The passivation performance, however, degraded and returned to as it was, in less than about 10 minutes at oven temperature and inlet pressure of about 200° C. and about 40 psi respectively. In contrast, PMP postcoating resulted in good peak shapes for subsequent organophosphonate headspace injections and also the performance remained consistent for 8 days of testing. Structurally PMP is different from the other phosphonates due to the presence of a phospho hydroxyl (P—O—H) bond rather than the phospho ester bond (P—O—C) found in DIMP. Apart from being a heavy phosphonate, PMP may poison the active sites because the P—O—H bond reacts with the active sites and replaces the hydrogen.

Without further elaboration, it is believed that one skilled in the art using the preceding description can utilize the invention to the fullest extent. The following examples are illustrative only, and not limiting of the disclosure in any way whatsoever.

EXAMPLES

Preparatory Example 1

Microcolumn Fabrication

Microfabrication started with a double side polished four inch (5-20 ohms-cm) p type silicon wafer from SiliconQuest (Santa Clara, Calif.). The wafer was coated on both sides with Shipley SPR220-7 photoresist at 3000 rpm. Double side photolithography was performed to obtain an image of 100 microns wide and 3 meters long channel on the front side and 210 microns port holes on the back side. A hard bake at about 140° C. was performed for about 30 minutes to withstand the further deep reactive ion etching 100 microns on the channel side and through access holes in silicon on the back side.

Four 3 meter long microcolumns were obtained from processing one silicon wafer. The resulting microcolumns were cleaned with Shipley Microposit Remover 1165 at 120° C. followed by a standard clean 1 (SC-1) at 73° C. Pyrex 7740 glass pieces of the size of silicon die are cut out from wafers using diamond wheel cutter, followed by an SC-1 clean. Silicon channels were anodically sealed with the cleaned

Pyrex glass at about 400° C. with 900 V bias. The bonded microcolumn was packaged in the manifold only after the deactivation step.

Preparatory Example 2

Deactivation of the Microcolumn

Three different deactivation procedures were performed; silylation, persilylation, and organosilicon hydride treatment. Silylation was performed with a 10% DMDCS ((Gelest, Boston, Mass.) solution in toluene, passed through the microcolumn heated at 100° C. for about 8 hours, followed by a toluene, methanol and ether rinse. The microcolumn was then dried under nitrogen flow prior to testing.

Persilylation and organosilicon hydride deactivation was performed using Ah3P (Gelest, Boston, Mass.) and DPT-MDS ((Fluka, Santa Clara, Calif.), respectively. The deactivation was performed by dynamically coating the surface with a one microcolumn length plug of neat reagent. A brass reservoir manifold containing the solution was attached on one of the access ports and the plug was pulled using a 26" Hg vacuum at the second access port. After the liquid plug evacuation the microcolumn was heat-treated in a vacuum annealer (300 microns Hg) at a rate of about 8° C. min^{-1} to about 375° C. and held at the final temperature for 4 hours. The vacuum annealer was purged with nitrogen for about 20 minutes before applying vacuum to ensure oxygen absence. The microcolumn was cooled to room temperature before exposing to atmosphere. The microcolumn was connected to 0.5 meter long fused silica transfer lines using a brass manifold as shown in FIG. 1C. A two ferrule design consisting of a polyimide ferrule deforming the polytetrafluoroethylene (PTFE) ferrule to achieve a leak-tight seal between the fused silica capillaries and the chip (see FIG. 1D). The packaged microcolumn was rinsed with one microcolumn volume of methanol and pentane at 25 µl/min followed by one microcolumn volume of air using a syringe pump.

Preparatory Example 3

Stationary Phase Coating

A 5% polar phase was chosen to achieve separation of phosphonates. The 4% (w/v) coating solution was prepared by dissolving OV-5 vi (Ohio Valley, USA) vi phase in pentane in a sonicator bath. Dicumyl peroxide (DCP) (Sigma Aldrich, Santa Clara, Calif.) in the form of 2% (w/v) toluene solution was added to the coating solution to achieve a final concentration of 0.2% (w/w) in the deposited stationary phase. The microcolumn was filled with the coating solution and dynamically driven out with air at a rate of 25 µl/min. The coated microcolumn was then connected to a conventional GC to perform cross-linking at about 140° C. for 1 hour with hydrogen flowing at a pressure of 5 psi. The conditioning of microcolumn was performed by heating the microcolumn to about 200° C. for 4 hours with hydrogen flow rate of 40 psi. Upon cooling the microcolumn, the fused silica connection lines were replaced with new deactivated fused silica lines. The later procedure ensured the true measurement of the microcolumn's performance. The fused silica legs were trimmed to the shortest length required for connection in a conventional GC.

Preparatory Example 4

Postcoating Treatments

Two post-microcolumn treatments were performed, one with PMP (Sigma Aldrich, Santa Clara, Calif.) and one with

Rejuv-8 (Sigma Aldrich. Santa Clara, Calif.). The PMP treatment was performed on a conventional GC at 110° C. by injecting 1 microliter of liquid splitlessly with a hydrogen flow at 40 psi followed by a stabilizing time of 1 hour with the hydrogen flowing. The microcolumn was reconditioned at 200° C. with 40 psi inlet pressure for 4 hours. The reconditioning end was checked with the presence of a stable FID baseline.

The resilylation treatment with Rejuv-8® was performed by four injections each one hour apart. Each injection consisted of 5 microliters of liquid at 100° C. with inlet pressure of 10 psi. The resilylation treatment was followed by reconditioning treatment stated earlier.

Specific Example 5

Microcolumn Testing

An Agilent 6893N GC/FID-MS, with 7683B autosampler was used for all the separations. Packaged microcolumn was placed in the GC and connected to the split inlet and FID using a Restek deactivated guard microcolumns. Hydrogen was used as carrier gas in all tests except when carrying out Agilent microcolumn testmix injection. Helium was used in the later case. Headspace injections of DIMP (Alfa Aesar, Ward Hill, Mass.) and n-octanol (Sigma Aldrich, Santa Clara, Calif.) were performed to quick-check microcolumn activity. DIMP was used a representative phosphonate tracer. Octanol was selected because it is a very sensitive probe for microcolumn deactivation problems. The deactivation optimization tests were performed on 35 cm long microcolumns injecting 5 µl headspace with a split of 50:1 and oven temperature and inlet pressure held at 75° C. and 5 psi respectively.

The effect of post-coating treatment on phosphonate activity was carried out on 3 meter long, OV-5 coated, Ah3P deactivated microcolumns by injecting 5 µl DIMP headspace with a split of 50:1 and microcolumn temperature and pressure at 110° C. and 20 psi, respectively. Detailed study of microcolumn activity was performed using DB-5 microbore microcolumn test mix supplied by Agilent (Santa Clara, Calif.). The 1 µl of test mix liquid was injected with a split of 1000:1. The inlet pressure adjusted to achieve a helium carrier gas velocity of 20 cm/s. The oven temperature was adjusted to 120° C. to achieve a retention factor of about 6 for tridecane.

The chromatograms were analyzed using Agilent's MSD-Chem data analysis software. Microcolumn plates were calculated using the tridecane peak in the Agilent microcolumn test mix injection as follows:

$$N = 5.54 \cdot \left(\frac{t_R'}{W_h} \right)^2 \tag{1}$$

where, t_R' is retention time of the tridecane minus methane retention time. W_h is width of the tridecane peak, taken at ½ the peak height.

Specific Example 6

Infrared Analysis

Fourier transform infrared spectroscopy (FTIR) was performed on silicon samples to further understand the effect of the PMP treatment. A double side polished four inch silicon wafer was spin coated with neat Ah3P solution at 3000 rpm for 40 seconds. The coated wafer was then heated in a vacuum

annealer as previously described for the microcolumn deactivation. OV-5 coating solution was prepared as mentioned earlier for microcolmn coating procedure in Preparatory Example 3, supra. Deactivated wafer pieces were spin coated with the coating solution at 3000 rpm followed by a cross-linking treatment in a vacuum annealer at 140° C. for 1 hour. PMP treatment of the coated silicon piece was performed by spin coating neat PMP solution at 3000 rpm followed by heat treatment at 200° C. in the vacuum annealer. PMP vaporization was found to be complete in a control experiment under these treatment conditions. The treated surfaces were analyzed using a Nicolet Nexus 670 FTIR in the transmission mode. IR Spectra was collected in the transmission mode with 64 scans from 800 to 4000 cm^{-1} with a resolution of 2 cm^{-1}. ACD/SpecManager software was used to perform suitable background correction to the IR spectrum.

Specific Example 7

Dynamic Coating of Stationary Phase for Microcolumn Preparation

Model Capillary Preparation

A 15 m long spool of square capillary (100 μm×100 μm I.D., 365 μm O.D., Polymicro Technologies) was passivated using a dynamic vapor-phase silylation method known in the art. Rejuv® (Sigma Aldrich, a commercial silylating mixture of n,O-bis(trimethylsilyl)acetamide, hexamethyldisilazane, and 1-(trimethylsilyl)imidazole) was used as the silylating reagent. Following the passivation the square capillary was cut into 1 m long sections for dynamic coating according to the design of experiments.

Coating Solution Preparation

5% polar stationary phase, OV-5 vinyl gum obtained from Ohio Valley Specialty Company (Marietta, Ohio) was chosen as the stationary phase due to its wide applicability. The coating solutions were prepared in hexamethyldisilazane treated 12×32 vials obtained from Alltech (#72670). The required amount of stationary phase was transferred to a vial and adequate quantity of 0.2 μm filtered pentane was injected into the capped vial using a syringe to produce the required concentration of coating solution. The stationary phase was dissolved by sonicating the vial for 20 minutes. Dicumyl peroxide (DCP) (Sigma Aldrich, >99%) in the form of freshly prepared 2% (w/v) pentane solution was added to the coating solution to achieve a DCP concentration of 1% (w/w of the stationary phase).

Mode-Column Coating Process

The column coating process was performed inside a conventional GC oven. As shown in FIG. 9, Panel A, 1 m and 3 m long capillaries (250 um I.D., 360 um O.D.) were used as pre-column and post-column buffer respectively, for flow restriction. The square capillaries were connected to the buffer capillaries using Teflon® tubing sleeve (Upchurch Scientific, F-243X) and a Swagelok ⅟16" union. The coating process proceeded by filling the coating solution in the square capillary plus the post-column buffer and then connecting the square capillary to the GC inlet via the pre-column buffer. The square column and the post-column buffer were immersed in a 22° C. water bath during the coating process. The GC inlet system was used to apply the coating pressure (split flow of 100:1 provided good stability and accuracy). After the coating solution exited the post-column buffer was disconnected and the carrier gas inlet pressure was pulsed to 20 psi for a short duration. This step allowed drying all the solvent post deposition. The GC inlet pressure was then set to 0.8 psi and the deposited stationary phase was cured by rapidly heating

the GC oven and holding at 110° C. for 10 minutes, followed by overnight treatment at 140° C. for complete curing. The next day columns were conditioned at 200° C. for 1 hour, cooled down to room temperature and trimmed to 0.8 m length for chromatographic evaluation.

Coated Column Tests

An Agilent 6893N GC/FID-MS equipped with 7683B auto-sampler was used for all the separations. The chromatograms were recorded using the MSD Chemstation software and processed using the Peakfit software (v4.12). Helium was used as the carrier gas in this paper. The injector temperature was held at 250° C. Methane injections were used to measure the average velocities. Isothermal test mixture was prepared using puriss-grade chemicals (GC standards) from Aldrich (Milwaukee, Wis.).

Isothermal chromatographic performances of the square columns were tested by isothermally separating C_{10} to C_{12} n-alkanes on the columns held at 70° C. A standard containing the alkanes (1000 ppm each) was prepared in an n-C_5 matrix and 1 μl of the standard was injected with a split of 1000:1 into the coated square capillary columns. The carrier gas velocity was maintained at 25 cm/s in all isothermal separation tests.

Temperature-programmed separation performances of the coated square columns were obtained by injecting 1 μl of a Grob's mix (Alltech, 41761) with a split of 1000:1. The coated square columns were held at 30° C. and ramped to 150° C. at the rate of 2.96° C./min. The carrier gas velocity was held constant at 28 cm/s in all temperature programmed separation tests.

Design of Experiment (DoE), Analysis, and Optimization

FIG. 9, Panel B, shows the diagram of dynamic coating and the coating variables that were varied in this example. FIG. 9, Panel C shows the adapted E-Chip software generated D-optimal design to test the different combinations of dynamic coating parameters viz. coating solution concentration and square root of the coating pressure, each as a continuous variable in the range of 0.3-10 (w/v) % and 0.8-1.8 psi, respectively. The ranges were restricted by the feasibility of conducting coating experiments. Outcomes of the coating process were measured in two chromatographic separation modes: retention times (t_R) and theoretical plate numbers (N) for C_{11} and C_{12} n-alkane peaks and resolution (R_S) for the latter peak pair were measured in the isothermal separation mode; elution temperatures (T) for methyl decanoate (E10) and methyl dodecanoate (E12) peaks and Trennzahl number (TZ) for the latter peak pair were measured in the temperature programmed separation mode. Theoretical plate number (N), Resolution (R_S) and Trennzahl numbers (TZ) were calculated by,

$$N = 5.54 \cdot \left(\frac{t_R}{W_h}\right)^2 \qquad (2)$$

$$R_S = \frac{2 \cdot (t_{R2} - t_{R1})}{w_{h1} + w_{h2}} \qquad (3)$$

$$TZ = \frac{t_{R2} - t_{R1}}{w_{h1} + w_{h2}} - 1 \qquad (4)$$

where, t_{R1} and t_{R2} are the retention times, and w_{h1} and w_{h2} are the peak widths at half height of peaks 1 and 2 respectively. The experimental data was fit to a quadratic model,

$$R = A_0 + A_1 \cdot c + A_2 \cdot p + A_3 \cdot c \cdot p + A_4 \cdot c^2 + A_5 \cdot p^5 \qquad (5)$$

where, R is the response variable, A_0-A_5 are model coefficients, c is the coating solution concentration, and p is the coating pressure.

Optimization of coating parameters was carried out by: simultaneous maximization of theoretical number of plates and resolution for isothermal separations, and maximization of Trennzahl number for temperature programmed separation.

Translation of DoE Results to Coat Micro-Columns

The dynamic coating parameters to obtain efficient columns were identified by optimization of isothermal and temperature-programmed elution characteristics (resolution, Trennzahl number, and theoretical plate numbers). The suitable concentration found could be directly utilized in coating micro-columns; however the coating pressure had to be translated to methane retention times that reflected the permeability of the micro-columns to be coated.

Design and Fabrication of Micro-Columns

Microfabrication started with a double side polished silicon wafer (4" diameter, 250 μm thick, 5-20 ohms-cm p-type) from Silicon Quest International. The wafer was sputter coated with 1000 Å thick aluminum on one side. The aluminum layer protected the silicon surface from getting damaged during the fabrication steps prior to anodic bonding. Shipley SPR220-7 photoresist was spin-coated on both sides of the wafer at 3000 rpm. Double side lithography was performed to obtain an image of micro-channels on the aluminum side and fluid transfer holes on the silicon side. The chrome mask set for lithography was fabricated by Photo Sciences Inc. using a laser pattern generator. Micro-channel mask consisted of four 3.2 cm×3.2 cm dies each filled with 100 μm wide and 3 m long micro-channel folded in a serpentine configuration. The second mask consisted of 210 μm wide fluid transfer holes for connecting the micro-channels from the bottom side. 10 micron wide crosses were designed in the masks to aid the alignment process. Exposed photoresist was developed in MIF327 developer. Overdevelopment with MIF327 was allowed to etch the underlying aluminum layer exposing the silicon surface for reactive ion etching. The patterned photoresist was baked at 140° C. for 30 minutes to withstand the plasma exposure in the reactive ion etching steps. Deep reactive ion etching was used to etch the channel patterns 100 μm deep and the access holes through the wafer. The wafer was diced during the latter step. The micro-column dies were cleaned with Shipley Microposit Remover 1165 at 120° C. followed by an aluminum etching in type A aluminum etchant (Transene company), and a standard clean 1 (SC-1) at 73° C. Pyrex® 7740 glass pieces approximately of the size of micro-column die were cut out from wafers using an IR laser and cleaned using an SC-1 clean procedure. Silicon micro-columns were anodically sealed with the cleaned Pyrex® glass at 400° C. with 900 V bias.

Micro-Columns Passivation

Organosilicon hydride passivation using phenyltris(dimethylsiloxy)silane (Ah3P) (Gelest, SIP6826) was performed. The passivation was performed by dynamically coating the surface with one column length plug of neat reagent. A brass reservoir manifold containing the solution was attached on one of the micro-column access ports and the plug was pulled using a 660.4 mm Hg vacuum at the second access port. After the liquid plug exited the micro-column was heat-treated in a vacuum annealer (300 microns Hg) at a rate of 8° C. min^{-1} to 375° C. and holding at the final temperature for 4 hours. The vacuum annealer was purged with nitrogen for 20 minutes before applying vacuum to ensure oxygen absence. The micro-column was cooled to room temperature before exposing to atmosphere.

Micro-Column Coating Process

The ends of the micro-column were connected to a 1 m and 3 m long fused silica capillary (100 μm I.D. and 200 μm O.D.,

Polymicro technologies, TSP100200) using Nanoports® (Upchurch Scientific, N-125S). Special fluorosilicone gaskets were used with Nanoports® to create a low dead volume connection. The coating solution from a gas tight syringe was pushed using mild hand pressure to fill the micro-column and buffer capillaries. The syringe was disconnected when four drops of coating solution left through post-column buffer capillary end. The pre-column buffer was attached to a GC inlet and the coating solution was driven out using calculated pressure corresponding to the required methane retention times. When the coating solution exited the post-column buffer capillary, the solvent from the coated stationary phase was removed by pulsing the inlet pressure to 20 psi for a short duration. Subsequently, the inlet pressure was reduced to 0.8 psi and the stationary phase was cross-linked and conditioned by heating the micro-column to 140° C. overnight.

Post-coating pinacolyl methylphosphonic acid (PMP) deactivation treatments was performed. The PMP treatment was performed on a conventional GC at 110° C. by injecting 1 μl of liquid PMP in the splitless mode (injector temperature of 250° C.) with a helium flow at 20 psi followed by a stabilizing time of 1 hour with the carrier gas flowing. The micro-column was reconditioned at 200° C. with 20 psi inlet pressure for 4 hours. The completion of reconditioning process was checked with the presence of a stable FID baseline. The connecting fused silica capillaries were replaced with Restek deactivated guard capillaries (100 μm I.D., 200 μm O.D., and 25 cm long, IP deactivated) and the latter was trimmed to the required minimum length prior to testing.

Design of Experiment Analysis

Chromatography was performed to compare the isothermal separation of alkanes and temperature programmed separation of Grob's mix obtained by changing the coating plug concentration or the coating pressure. Increasing the coating pressure from 1.1 psi to 1.8 psi while holding the coating solution concentration constant at 3.5 (w/v) % produced square columns with higher retention times in isothermal and temperature programmed separation. The isothermal retention times of C_{10}, C_{11}, and C_{12} increased from 6.5, 9.8, and 13.3 seconds respectively to 6.8, 10.2, and 13.7 seconds respectively. The temperature programmed retention times of E10, E11, and E12 increased from 6.45, 9.76, and 13.27 minutes respectively to 6.81, 10.18, and 13.73 minutes respectively. Similarly increasing the coating solution concentration from 3.5 (w/v) % to 6.76 (w/v) % while holding the coating pressure constant at 1.1 psi also produced square column with higher retention times in isothermal and temperature programmed separation. The isothermal retention times of C_{10}, C_{11}, and C_{12} increased from 6.5, 9.8, and 13.3 seconds respectively to 8.3, 11.8, and 15.4 seconds respectively. The temperature programmed retention times of E10, E11, and E12 increased from 6.45, 9.76, and 13.27 minutes respectively to 8.27, 11.76, and 15.38 minutes respectively.

The separation parameters: retention times (t_R), effective theoretical plate numbers (N) and resolution (R_S) for C11 and C12 peaks for isothermal separations; elution temperatures (T), and Trennzahl numbers (TZ) for temperature-programmed separations, were modeled with a quadratic equation. Model surface plots were generated which predicted the isothermal retention times of C_{11} (A) and C_{12} (B) on square capillaries coated with various coating pressures and coating solution concentrations. The quadratic model was found to predict the C_{11} and C_{12} isothermal retention times with an R-squared value of 0.92. The fitting routine predicts that concentration, concentration-squared and pressure-squared terms play the most important role in determining the retention times. Increasing the coating concentration was found to

increase the isothermal retention times regardless of the coating pressure; however increasing the coating pressure led to a point of minimum retention at all concentrations. Increasing the coating pressure past this value of minimum retention was found to increase the retention times. The coating pressure corresponding to the minimum retention point was found to be about 1.5 psi in the low coating concentration range (0.3 to 2 (w/v) %) and was found to shift to 1.3 psi in the high coating concentration range (7-10 (w/v) %).

A plot of the model surface and experimental data for the effective number of theoretical plates (N) was calculated based on the isothermal C_{11} and C_{12} elution as a function of the dynamic-coating pressure and concentration used to coat the square capillaries. The quadratic model was found to predict N for C_{11} and C_{12} isothermal elution with an R-squared value of 0.92 and 0.95 respectively. The fitting routine predicts that concentration and concentration squared terms play the most important role in determining the theoretical plate numbers. The model predicts that the value of N for square capillaries coated with less concentrated solutions increased from 16 to 180 plates/m with the increase in coating pressure from 0.8 to 1.8 psi; however the effect of coating pressure on N was found to be negligible as the coating concentration increased above 3 (w/v) %. N was found to increase with the increase in coating solution concentrations and to plateau at N values of 3500-4000 plates/m with higher coating concentrations irrespective of the coating pressure.

A plot of model surface and experimental data for the resolution between the isothermally eluted C_{11} and C_{12} peaks as a function of dynamic coating pressure and concentration used to coat the square columns was generated. The quadratic model was found to predict the resolution between the C_{11} and C_{12} peaks with an R-squared value of 0.97. The fitting routine predicts that concentration, concentration multiplied by pressure, and concentration squared terms play the most important role in determining the resolution. The resolution was found to be independent of the dynamic coating pressure except at low coating solution concentrations. The resolution was found to increase with the increase in coating solution concentration and then plateau to a value between 16.5 and 18.5 above 6 (w/v) % concentrations.

A plot of the model surface and experimental data for elution temperatures corresponding to the E10 and E12 as a function of dynamic coating pressures and concentrations was generated. The quadratic model was found to predict the elution temperatures for E_{11} and E_{12} during the temperature programmed separations with an R-squared value of 0.9. The elution temperatures were found to increase as the coating concentration was increased. The elution temperatures were found to increase on increasing the coating pressures at low concentrations; however at higher coating concentrations, the elution temperatures were not found to depend on the coating pressure.

The model surface plot and experimental data for the Trennzahl numbers (TZ) corresponding to the E10 and E12 fatty acid methyl ester elution on square columns coated with different coating pressures and concentrations was generated. The quadratic model was found to predict the Trennzahl numbers for E11 and E12 temperature programmed elution with an R-squared value of 0.66. The model does not adequately predict the TZ value but predicts only the trend in the experimental data. Regardless of the coating pressure, the change in coating concentration from 3.5 to 10 w/v % changes the TZ value changes from about 13 to about 20. Changing the pressure had minor effect on the TZ values

particularly at low concentrations; however at higher concentrations, the TZ values were found to decrease with increasing coating pressures.

The optimization was carried out by simultaneously maximizing theoretical number of plates for C_{11} and C_{12} peaks, the resolution between the latter peaks, and the Trennzahl number for E11 and E12 peak pair. The optimization routine predicted that the optimum point lies at a coating concentration of 10 w/v % and coating pressure of 0.9 psi. Due to the insufficient fit of the model to the Trennzahl numbers, exclusion of the latter was also tried in the optimization process; however there was no difference in the optimum point values. The quadratic model predicted an R_S value of 18.46 within 95% confidence intervals of 20.51 and 16.39. The predicted N_{C11} and N_{C12} values were 4165 and 3854 within the 95% confidence intervals of (2754, 5866) and (2832, 5032). FIG. 10 shows the isothermal (A) and temperature-programmed (B) separation chromatograms obtained on a square capillary coated with the optimized dynamic coating parameters. The experimental values of theoretical plate numbers for the C_{11} and C_{12} peaks and the resolution between the pair of latter peaks were found to be 2664, 3003, and 16.95.

Translation of DoE Results to Coat Micro-Columns

Average velocity of 1.03 cm/s was found on the square capillary setup including the buffer columns at an inlet pressure of 0.9 psi. Translation of DoE findings to micro-column coating was achieved by using the coating pressure that was required to obtain a velocity of 1.03 cm/s on the micro-column setup. FIG. 11 shows the C_{10}-C_{12} n-alkane separation chromatogram on a micro-column coated with optimized conditions. The experimental values of theoretical plate numbers for the C_{11} and C_{12} peaks and the resolution between the pair of latter peaks were found to be 8311, 10742, and 29.46. Temperature programmed separation on coated micro-columns yielded a TZ of 19 between E10 and E12.

This example characterized the dynamic coating of stationary phase in the square DRIE microfabricated columns using model square fused silica capillaries. Optimization of the model square column coating parameters to obtain high N, R_S, and TZ values suggests that dynamic coating should be performed with high coating solution concentrations and lower coating pressures.

Experiments with higher concentrations required high pressures to fill the 100 μm×100 μm I.D, 1 m long square column plus the 3 m long post-column buffer during the coating process. This example showed that a maximum concentration of 10 (w/v) % for the OV-5 vi gum could be safely used with leakage. A minimum coating pressure of 0.8 psi accurately using a conventional-GC inlet was applied. The optimization routine resulted in an optimum coating pressure and concentration of 0.9 psi and 10 w/v % respectively. The model square column coated with the optimized dynamic coating parameters produced theoretical number of plates for C_{11} and the resolution between C_{11} and C_{12} peaks during the isothermal separation within the 95% confidence interval of that predicted by the quadratic model. However the number of theoretical plates for C_{12} peak was below that predicted by the model. This could have occurred due to the error in preparing accurate coating solution concentrations. The design of experiments carried out on square fused silica capillaries was found to be successfully transferred to making high performance micro-columns.

The general trend in the separation results from columns coated with different coating pressures and concentrations was found to be congruent with the theoretical predictions. The retention times of alkanes (C_{11} and C_{12}) in isothermal separations and fatty acid methyl esters (E10 and E12) in

temperature programmed separations increased with the increase in coating solution concentration. This confirms the increase in stationary phase film thickness on increasing the coating solution concentration. The retention times in temperature programmed separations are also found to constantly increase as a function of the coating pressure and are in agreement to what the theoretical coating equations predict. However the isothermal n-alkane retention times were not found to be an increasing function of coating pressure in the tested range. The model surface for isothermal retention times predicts that there exists a minimum retention time point as the coating pressure is varied.

The examples given above are merely illustrative and are not meant to be an exhaustive list of all possible embodiments, applications or modifications of the invention. Thus, various modifications and variations of the described methods and systems of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention. Although the invention has been described in connection with specific embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the described modes for carrying out the invention which are obvious to those skilled chemical and/or mechanical engineering or in the relevant fields are intended to be within the scope of the appended claims.

The disclosures of all references and publications cited above are expressly incorporated by reference in their entireties to the same extent as if each were incorporated by reference individually.

What is claimed is:

1. A Gas chromatography (GC) column, comprising:
a plurality of column walls each having a deactivated inner surface;
a stationary phase layer deposited on the deactivated inner surface of said plurality of column walls;
a plurality of binding sites in said stationary phase layer; and
a post-coating molecule bound to at least one of said plurality of binding sites in said stationary phase layer;
wherein the post-coating molecule is one or more compounds selected from the group consisting of a thiol, a phosphine, an amine,
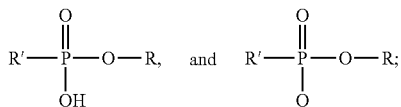
wherein R and R' are linear, branched, or substituted hydrocarbons.

2. The GC column of claim 1, wherein the inner surface of said plurality of column walls has been deactivated with a compound selected from the group consisting of DMDCS, Ah3P, and DPTMDS.

3. The GC column of claim 1, wherein said stationary phase layer has a thickness of about 0.1 μM.

4. The GC column of claim 1, wherein said stationary phase layer is uniformly spread over the inner surface of said plurality of column walls.
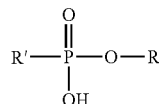
5. The GC column of claim 1, wherein said plurality of column walls has a serpentine configuration.

6. The GC column of claim 1, wherein said plurality of column walls are rounded.

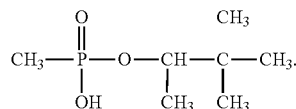7. The GC column of claim 1, wherein said post-coating molecule comprises a structure of Formula I:

Formula 1

where R and R' are linear, branched, or substituted hydrocarbons.

8. The GC column of claim 1, wherein the post-coating molecule comprises the structure of Formula II:

Formula 2

9. A method for preparing a gas chromatograph (GC) column, said method comprising the steps of
deactivating a plurality of walls of a GC column;
depositing a stationary phase in the GC column; and
treating the GC column with a molecule such that the molecule binds to active sites in the stationary phase of the column;
wherein the molecule is one or more compounds selected from the group consisting of an acid including hydrocarbon ligands, a base including hydrocarbon ligands, a thiol, a phosphine, and an amine.
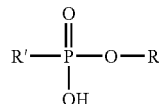
10. The method of claim 9, wherein the stationary phase in said depositing step is applied at a pressure of about 0.9 psi and at a concentration of about 10 w/v %.

11. The method of claim 9, wherein the deactivating step comprises a method selected from the group consisting of silylation, perisilylation, and deactivation using an organosilicon hydride.

12. The method of claim 11, wherein the silylation is performed using DMDCS, the perisilylation is performed using Ah3P, and the deactivation with the organosilicon hydride is performed using DPTMDS.

13. The method of claim 9, wherein the molecule in said treating step comprises a structure of Formula I:
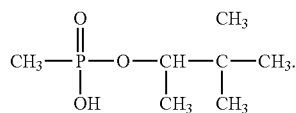

Formula 1

where R and R' are linear, branched, or substituted hydrocarbons.

14. The method of claim **13**, wherein the molecule comprises the structure of Formula II:
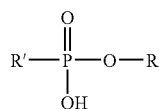
Formula 2

$$CH_3 - \overset{\displaystyle \overset{O}{\|}}{\underset{\displaystyle \underset{OH}{|}}{P}} - O - \overset{\displaystyle \underset{\displaystyle \underset{CH_3}{|}}{CH}}{} - \overset{\displaystyle \overset{CH_3}{|}}{\underset{\displaystyle \underset{CH_3}{|}}{C}} - CH_3.$$

15. A gas chromatograph (GC) column prepared by the method of claim **9**.

16. The GC column of claim **15**, wherein the molecule in said treating step comprises a structure of Formula I:
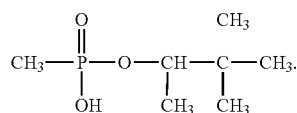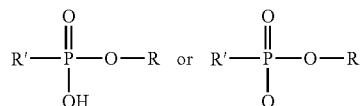
Formula 1

$$R' - \overset{\displaystyle \overset{O}{\|}}{\underset{\displaystyle \underset{OH}{|}}{P}} - O - R$$

where R and R' are linear, branched, or substituted hydrocarbons.

17. The GC column of claim **15**, wherein the molecule comprises the structure of Formula II:

Formula 2

$$CH_3 - \overset{\displaystyle \overset{O}{\|}}{\underset{\displaystyle \underset{OH}{|}}{P}} - O - \overset{\displaystyle \underset{\displaystyle \underset{CH_3}{|}}{CH}}{} - \overset{\displaystyle \overset{CH_3}{|}}{\underset{\displaystyle \underset{CH_3}{|}}{C}} - CH_3.$$

18. The GC column of claim **15**, wherein the molecule comprises the structure of Formula III:

$$R' - \overset{\displaystyle \overset{O}{\|}}{\underset{\displaystyle \underset{OH}{|}}{P}} - O - R \quad or \quad R' - \overset{\displaystyle \overset{O}{\|}}{\underset{\displaystyle \underset{O}{|}}{P}} - O - R$$

where R and R' are linear, branched, or substituted hydrocarbons.

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