

This article was downloaded by:

On: 24 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Journal of Liquid Chromatography & Related Technologies

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597273>

Reaction of Silica Gel with Trimethylsilyl Donors Using Conditions Useful for End-Capping HPLC Bonded Phase Packings

Kenneth D. Mc Murtrey^a

^a Department of Chemistry, University of Southern Mississippi Hattiesburg, Mississippi

To cite this Article Murtrey, Kenneth D. Mc(1988) 'Reaction of Silica Gel with Trimethylsilyl Donors Using Conditions Useful for End-Capping HPLC Bonded Phase Packings', *Journal of Liquid Chromatography & Related Technologies*, 11: 16, 3375 – 3384

To link to this Article: DOI: 10.1080/01483918808082260

URL: <http://dx.doi.org/10.1080/01483918808082260>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

REACTION OF SILICA GEL WITH TRIMETHYLSILYL DONORS UNDER CONDITIONS USEFUL FOR END-CAPPING HPLC BONDED PHASE PACKINGS

KENNETH D. MC MURTREY

*Department of Chemistry
University of Southern Mississippi
Hattiesburg, Mississippi 39406-5043*

ABSTRACT

Several trimethylsilyl (TMS) donors including bis-N,O-trimethylsilylacetamide (BSA), bis-N,O-trimethylsilyltrifluoroacetamide (BSTFA), hexamethyldisilane (HMDS), trimethylchlorosilane (TMCS) with and without pyridine, 2-trimethylsiloxypent-2-en-4-one (TMSOP), trimethylsilyldimethylamine (TMSDMA), and trimethylsilylimidazole (TMSIM) were reacted with 60 Å silica. TMSIM at 60 °C with reaction times of one hour or less gave coverage of silica gel equivalent to that provided by refluxing TMCS and pyridine in toluene for 67 hrs. Reactivity of the TMS donors studied may be ranked in the following order: TMSIM > TMSDMA > BSTFA > BSA > TMCS > TMSOP > HMDS. TMSIM appears to be the reagent of choice for end-capping of alkyl bonded HPLC phases.

INTRODUCTION

Reversed phase liquid chromatography packings are usually produced by bonding reactive silanes to silica gel particles. The

chemistry of this process involves reaction of silanol groups at the surface of the silica gel particles with chloro or alkoxy substituted silanes, producing a Si-O-Si-C linkage from the inorganic silica to the organic moiety. Subsequently, the packing material is frequently "end-capped" by reaction with a trimethylsilyl donor. In most cases trimethylchlorosilane (TMCS) is the end-capping reagent chosen. TMCS has been used alone or with a base (usually pyridine) which apparently functions as an acid scavenger or as a catalyst.

The goal of end-capping is to remove as many residual silanols as possible. It is well known that no more than half of the 7 to 8 $\mu\text{mole/g}$ of surface silanol groups present in totally hydrated silica react under conditions normally employed (1). Some of these unreacted silanols are available for interactions with solute molecules which can lead to nonideal behavior with attendant diminished efficiencies, particularly for basic analytes.

As mentioned above, the usual reagent used in end-capping is trimethylchlorosilane, which is employed almost to the exclusion of other TMS donors. Many potential TMS donors exist. The practice of gas chromatography has led to the development of a number of reagents for preparation of TMS derivatives of substances which have low volatility because of polar functional groups (alcohols, phenols, etc.). These reagents possess a variety of characteristics. For example, the byproducts of reaction of some donors are acidic (e.g., TMCS produces HCl during reaction), some are basic (trimethylsilylimidazole (TMSIM) and trimethylsilyldimethylamine (TMSDMA) give imidazole and dimethylamine, respectively), while others are neutral (bis-N,O-trimethylsilylacetamide (BSA) and bis-N,O-trimethylsilyltrifluoroacetamide (BSTFA) produce acetamide and trifluoroacetamide, respectively). TMS donors also differ markedly in reactivity. Although reactivity also depends on the substance being derivatized, in general the following order prevails (2):

TMSIM > BSTFA) > BSA > TMSDMA > TMCS (with base) > hexamethyldisilane (HMDS).

It is surprising that so few of the potential TMS donors have been used to end-cap HPLC stationary phases, and that a study of their relative reactivities does not appear to have been made.

In this paper we describe stationary HPLC phases which were prepared by reacting a number of TMS donors with silica gel under conditions appropriate for end-capping of HPLC packings.

EXPERIMENTAL

Chemicals: TMS donors were purchased from Petrarch Systems (Bristol, PA), other materials were purchased from commercial suppliers. Silica gel marketed for thin layer chromatography (Analtech, Newark, DE) which had been separated into narrow particle size fractions by a process described elsewhere (3) was used in this study. The silica is irregular shaped particles of $d_p = 7 \pm 2 \mu\text{m}$ with a nominal pore size of 60 \AA and surface area of $455 \text{ m}^2/\text{g}$ determined using the method of Sears (4). The silica gel was maintained at $150 \text{ }^\circ\text{C}$ for at least 12 hrs and cooled in a vacuum dessicator at reduced pressures prior to bonding reactions.

Reaction Conditions: Most bonding reaction mixtures consisted of silica (2.0 g) and TMS donor in 4-fold excess (calculated assuming $8 \mu\text{mole/g}$ of silanol groups). The mixtures were maintained at $60 \text{ }^\circ\text{C}$ for one hour in 5 inch culture tubes and the silicas obtained in this way were washed 5 times with methanol. Tubes containing TMS donors which did not produce gaseous byproducts were sealed using teflon-faced screw caps. There was no appreciable increase in pressure inside the sealed tubes during reaction. TMS donors which produce gaseous products (TMCS and TMSDMA, for example) were reacted with silica in culture tubes which were equipped with drying tubes containing anhydrous calcium sulfate. TMSOP, which is a solid, was dissolved in 5.0 ml of dry toluene before reaction.

Reaction between TMSIM and silica was studied using modifications of the above conditions. In one series of reactions, mixtures (2.0 g silica, 4.72 ml TMSIM) were maintained at 60 °C for 15, 30 min, 24, 48, and 96 hours to study the effect of time. In a subsequent series of reactions, the above mixture of silica and TMSIM was heated at 100 or 195 °C for one hour. In addition, a larger scale reaction consisting of 20.0 g of silica gel and 47.2 ml of TMSIM was refluxed at 220 °C for one hour.

A reference coated silica gel was prepared according to conditions which have been reported to give "the highest possible coverage" of Zipax silica gel by TMS groups "provided reactions times of more than 48 hrs are employed (5)." In this reaction 20.0 g of silica, 50 ml of TMCS, and 100 ml of toluene were refluxed for 67 hours. The resulting material was collected by vacuum filtration, washed with 200 ml each toluene, methylene chloride, methanol, 1:1 methanol:water, water, and acetone and air dried.

Table 1

Donor	Capacity Factor					Coverage		
	A	NMA	DMA	Bz	To1	%C	%H	$\mu\text{mole}/\text{m}^2$
HMDS ^a	0.73	1.05	1.41	1.27	1.62	----	----	----
BSA ^a	1.34	2.45	3.72	3.55	5.09	----	----	----
BSTFA ^a	1.36	2.50	3.79	3.62	5.17	3.29	1.14	2.15
TMSDMA ^a	1.34	2.57	4.01	3.81	5.56	3.03	0.97	1.97
TMSOP ^b	1.08	1.83	2.54	2.46	3.34	2.62	1.12	1.69
TMCS ^a	1.09	1.82	2.57	2.50	4.03	2.22	0.97	1.42
TMCS/Py. ^a	1.06	1.76	2.54	2.44	3.38	----	----	----
TMCS/Imid. ^a	1.35	2.76	4.51	4.23	6.45	4.07	1.26	2.71
TMCS/Py/tol. ^c	1.48	2.90	4.65	4.40	6.57	4.70	1.38	3.17
TMSIM ^a	1.48	2.97	4.80	4.54	6.86	4.50	1.39	3.02

^a60 °C, 1 hour

^bin 5.0 ml toluene, 60 °C, 1 hour

^crefluxed 67 hours

Packing of HPLC Columns: Silica samples (ca. 2.0 g) were slurried in methanol and packed with downward flow into 4.6 x 150 mm stainless steel columns using acetone as a packing fluid at 8500 psi. Water (100 ml) was pumped through the columns to free them from acetone.

Evaluation of HPLC Columns: Columns were evaluated using five solutes: aniline, N-methylaniline, N,N-dimethylaniline, benzene, and toluene. Mobile phases consisting of 0.05 M $\text{NH}_4\text{H}_2\text{PO}_4$ in 40% CH_3CN were used at a flow rate of 1.0 ml/min. Sodium nitrate was used as a void volume marker for determination of capacity factors. Elemental analyses were performed by Galbraith Laboratories (Knoxville, TN).

Hydrolysis of Packings: Water at 60 °C was pumped through selected HPLC columns at a flow of 2 ml/min. Columns were evaluated from time to time using the conditions described above.

RESULTS AND DISCUSSION

Capacity factors for aniline (A), N-methylaniline (NMA), N,N-dimethylaniline (DMA), benzene (Bz), and toluene (Tol); the % carbon and hydrogen loading; and coverage of bonded packings synthesized using several TMS donors are given in Table 1. As may be seen, the reagents used differ markedly in their reactivities. Under comparable conditions (60 °C, ambient pressure, 1 hr) it is evident that TMSIM is considerably more powerful as a TMS donor than any other of the reagents tested.

The reaction of TMSIM with silica gel at 60 °C appears to be very rapid. A series of reactions conducted using reaction times from 15 minutes to 96 hours indicated that coverage of the silica (as evidenced by capacity factors of the five test solutes) was constant for all columns prepared. It seems probable that repetition of the experiments leading to the data in Table 1 at times of 15 min or less would give even more dramatic evidence of the relative reactivity of TMSIM compared to the other TMS donors.

The of reactivity of the TMS donors tested with silica gel may be ranked as follows:

TMSIM > TMSDMA > BSTFA > BSA > TMCS > TMSOP > HMDS

Reactivity of TMCS can be modified by addition of a base to the reaction mixture. At high temperatures over long reaction times pyridine is efficient, however, under the more mild conditions and short reaction times employed, addition of pyridine did not increase the reaction with silanols. A mixture of TMCS and imidazole, in contrast, provided coverage which was nearly as complete as TMSIM itself. It seems likely that TMCS and imidazole reacts to generate TMSIM in situ.

Inspection of the data in Table 1 also suggests that the relationship between the capacity factor of a solute and % carbon bonded to the silica gel is subject to some variation. The relationship between capacity factor of toluene and % C for a number of bonded phases is illustrated in Figure 1. The bonded phases used to construct this figure were all alkylsilyl derivatized silica. Although the general relationship between k' and % C is clear, it is also clear that other factors are operating. This is not surprising since retention of a solute must depend on the microenvironment at the surface of the stationary phase particle. The percent of carbon incorporated during bonding reactions should be proportional to the number of sterically accessible silanols present at the surface of the unreacted silica. Since steric requirements for reaction of an alkyl donor with a silanol may be different from the steric requirements for solute interaction with a bonded phase during chromatography some variation should be expected. It is clear, however, that retention does follow % C as a general trend. This trend is followed whether the bonded phase contains TMS, n-butyl, octyl, octadecyl groups, or mixtures of more than one of these species (end-capped material).

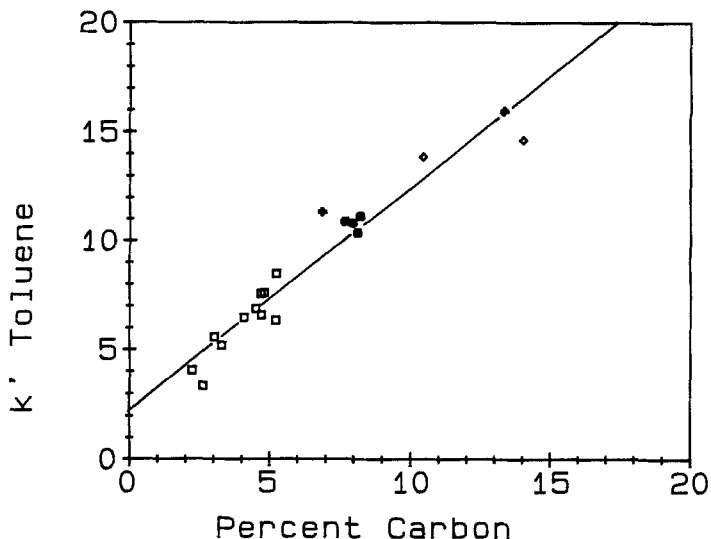


Figure 1. Variation of k' of toluene with percent carbon for TMS (\square), n -butyldimethylsilyl (\circ), n -octyldimethylsilyl (\bullet), and n -octadecyldimethylsilyl (\diamond) bonded phase columns. Mobile phase of $0.05\text{ M NH}_4\text{H}_2\text{PO}_4$ in 40% aqueous acetonitrile used for all determinations. The solid line is the linear least squares best fit. Actual best line would be a curve passing through the origin.

As shown in Figure 2, an increase in temperature of reaction from 60°C to 195°C was accompanied by an increase in both capacity factors for all solutes and the percent carbon bonded to the silica gel. Further reaction temperature increase to 220°C , in contrast, provided no further increase in percent carbon but gave a decrease in capacity factor for all solutes studied. This decrease could arise from at least two possible sources. First, the rather extreme reaction conditions could be acting to modify the surface of the silica gel by dehydration or loss of TMSOH groups. A second possibility is that the trimethylsilyl groups may be present in such concentration that steric interactions between them affect the interaction of solute molecules with the stationary phase. If the latter possibility is operating,

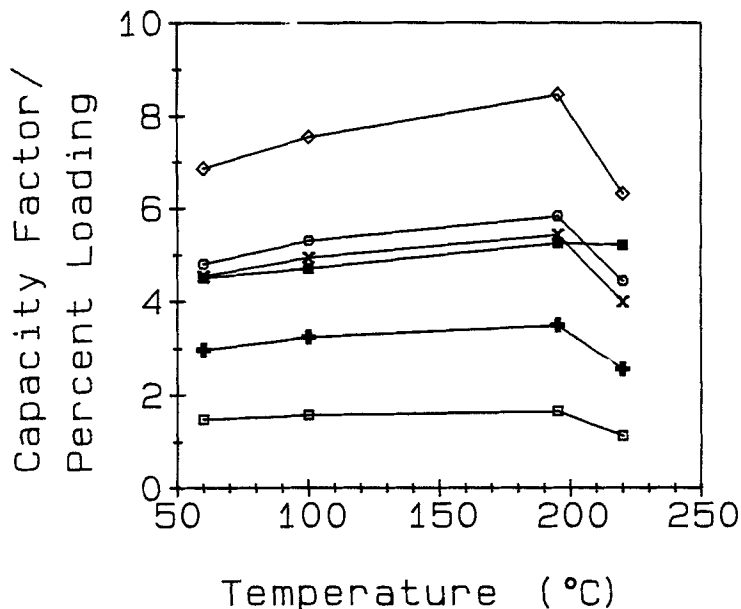


Figure 2. Variation of K' of test substances and % carbon incorporated on TMS bonded phase packings synthesized by reacting TMSIM with silica gel at different temperatures. Capacity factors for aniline (\square), N-methylaniline (\times), N,N-dimethylaniline (\circ), benzene (\times), and toluene (\diamond) were determined using conditions as in Figure 1. Percent carbon (\blacksquare) was measured by elemental analysis.

controlled hydrolysis of some of the TMS groups at the surface of the silica should lead to increases in k' values. Columns exposed to controlled hydrolysis at 60 °C showed no evidence of an increase in k' values for the test substances. Furthermore, it was determined that refluxing silica gel dried at 150 °C overnight with TMSIM produces considerable amounts of trimethylsilyl alcohol, the product expected if dehydration is occurring. The observed decrease in k' values for TMS bonded phases prepared at high temperatures appears to arise from changes in the silica gel induced by the energetic conditions employed.

CONCLUSION

The results presented above indicate that TMSIM is much more effective as an end-capping reagent than the frequently employed TMCS or TMCS with pyridine. Indeed, TMSIM at a temperature of 60 °C with a reaction time of less than one hour gives comparable coverage of silanols as TMCS and pyridine in refluxing toluene after 67 hours of reaction. Furthermore, no hydrogen chloride fumes are produced when TMSIM is used and the products of the reaction are easily removed by washing with organic solvents. While TMSIM is more expensive than TMCS it may be generated in situ by a mixture of TMCS and imidazole to give essentially equivalent coverage to that provided by the preformed reagent.

ACKNOWLEDGEMENT

The research described in this account was supported in part by a grant from the Institute of General Medical Sciences of the National Institutes of Health, grant number R15 GM38704.

REFERENCES

- (1) Unger, K.K., Porous Silica, Elsevier, Amsterdam, 1979, chapter 3.
- (2) Poole, C.F., Recent Advances in the Silylation of Organic Compounds for Gas Chromatography, in, Handbook of Derivatives for Chromatography, Blau, K., and King, G.S., eds., Heyden, London, 1978, p. 158.
- (3) McMurtrey, K.D., and DesLauriers, P.J., Size Fractionation of Thin-Layer Silica Gel by Sedimentation for Liquid Chromatography, Anal. Chem., 55, 396(1983).
- (4) Sears, G.W., Determination of Specific Surface Area of Colloidal Silica by Titration with Sodium Hydroxide, Anal. Chem., 30, 1981(1956).

- (5) Kohler, J., Chase, D.B., Farlee, R.D., Vega, A.J., and Kirkland, J.J., Comprehensive Characterization of Some Silica-Based Stationary Phases for High-Performance Liquid Chromatography, *J. Chromatogr.*, **352**, 275(1986).