

CHROMSYMP. 771

## ROLE OF THE FUNCTIONAL GROUP IN *n*-OCTYLDIMETHYLSILANES IN THE SYNTHESIS OF C<sub>8</sub> REVERSED-PHASE SILICA PACKINGS FOR HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY

K. D. LORK and K. K. UNGER\*

*Institut für Anorganische Chemie und Analytische Chemie, Johannes Gutenberg-Universität, 6500 Mainz (F.R.G.)*

and

J. N. KINKEL

*E. Merck, Chemical Reagents Division, R & D Chromatography, 6100 Darmstadt (F.R.G.)*

---

### SUMMARY

C<sub>8</sub> reversed-phase packings have been synthesised by reaction of a 25-nm pore-size high-performance liquid chromatographic silica (10 μm, *a<sub>s</sub>*(BET) = 297 m<sup>2</sup> g<sup>-1</sup>) with 2,4-lutidine as base and dichloromethane and N,N-dimethylformamide as solvents, or without solvents and with the following silanes: *n*-octyldimethylchlorosilane (C<sub>8</sub>-Cl), *n*-octyldimethylhydroxysilane (C<sub>8</sub>-OH), *n*-octyldimethylmethoxysilane (C<sub>8</sub>-OCH<sub>3</sub>), *n*-octyldimethylethoxysilane (C<sub>8</sub>-OC<sub>2</sub>H<sub>5</sub>), *n*-octyldimethyl(dimethylamino)silane [C<sub>8</sub>-N(CH<sub>3</sub>)<sub>2</sub>], *n*-octyldimethyl(trifluoroacetoxy)silane (C<sub>8</sub>-OCOCF<sub>3</sub>), and bis-(*n*-octyldimethylsiloxane) (C<sub>8</sub>-O-C<sub>8</sub>).

C<sub>8</sub>-Cl, C<sub>8</sub>-OH and C<sub>8</sub>-OCH<sub>3</sub> each form a reactive intermediate with 2,4-lutidine, favouring the reaction with the hydroxyl groups of the silica. In the C<sub>8</sub>-Cl reaction with silica, an amount of water larger than half of the stoichiometric amount of C<sub>8</sub>-Cl present in the starting reaction leads to a drastic decline in the ligand density of bonded C<sub>8</sub> groups. This is associated with the formation of C<sub>8</sub>-OH, which concurrently reacts with the remaining C<sub>8</sub>-Cl to form C<sub>8</sub>-O-C<sub>8</sub>, the latter exhibiting an extremely low reactivity. The highest reactivity of the silanes studied was observed for C<sub>8</sub>-N(CH<sub>3</sub>)<sub>2</sub>, since this already contains a reactive Si-N bond and furthermore eliminates the volatile dimethylamine, which is a co-product of silanization.

The ligand density of the bonded C<sub>8</sub> groups in the reaction of C<sub>8</sub>-N(CH<sub>3</sub>)<sub>2</sub> with silica was affected scarcely at all by the thermal pretreatment temperature (up to 800 K) of the silica, and the hydroxyl group concentration of the silica showed an approximately linear decrease at pretreatment temperatures of 500–900 K. Under comparable conditions, the reactivities of the silanes followed the sequence C<sub>8</sub>-N(CH<sub>3</sub>)<sub>2</sub> > C<sub>8</sub>-OCOCF<sub>3</sub> > C<sub>8</sub>-Cl ≧ C<sub>8</sub>-OH ≈ C<sub>8</sub>-OCH<sub>3</sub> ≈ C<sub>8</sub>-OC<sub>2</sub>H<sub>5</sub> ≧ C<sub>8</sub>-O-C<sub>8</sub>, with a maximum ligand density of 4.10 μmol m<sup>-2</sup> for C<sub>8</sub>-N(CH<sub>3</sub>)<sub>2</sub>. In accordance with their reaction mechanisms, distinct patterns in the course of the ligand densities achieved by the silanes as a function of the reaction temperature were obtained.

## INTRODUCTION

The past ten years have seen a variety of different procedures recommended for the synthesis of reversed-phase silica packings for high-performance liquid chromatography (HPLC), for which organosilanes of various *n*-alkyl chain-lengths are commonly employed.

Two bonding strategies have attracted the most interest with respect to the preparation of defined and reproducible reversed-phase silicas. The first involves the reaction of *n*-alkylsilanes of the types  $\text{RSiX}_3$  and  $\text{R}_2\text{SiX}_2$  ( $\text{X} = \text{chloro}$  or  $\text{alkoxy}$ ) with silicas under anhydrous or even hydrous conditions<sup>1-19</sup>. As a consequence of the stoichiometry and successive reactions, the newly formed hydroxyl groups at the surface of these packings were capped by a second silanization step prior to their use in reversed-phase HPLC. As monitored by  $^{29}\text{Si}$  and  $^{13}\text{C}$  NMR cross polarization magic angle spinning (CP MAS) spectroscopy, the silicas modified by  $\text{R}_2\text{SiX}_2$  and  $\text{RSiX}_3$  silanes exhibit a highly multifunctional surface pattern, which makes it difficult to obtain good reproducibility of the products<sup>20</sup>. The second approach uses the reaction of *n*-alkylmonochlorosilanes of the type  $\text{R}_3\text{SiX}$ , whereby the organosilyl moiety is attached by a single surface bond and only the corresponding disiloxane is formed as a by-product<sup>21-25</sup>. In order to overcome the relatively low reactivity of monochlorosilanes, other reactive silanes have been preferentially used in silanization reactions, *e.g.* dimethylaminosilanes<sup>26,27</sup>, trifluoroacetoxysilanes<sup>28,29</sup>, and silyl enolates of acetylacetone<sup>30</sup>. Furthermore, the usefulness of catalysts in the reaction of monochlorosilanes has been investigated<sup>29</sup>. Recently, a third strategy has been advocated, involving the generation of grafted, dense hydrophobic polymer coatings at the silica surface<sup>31</sup>.

To date, studies detailing the effect of the reactive functional group, X, of the silane,  $\text{R}_3\text{SiX}$ , in the synthesis of reversed-phase packings have been limited. This paper reports on the reaction of a 25-nm pore-size HPLC silica with a series of silanes, namely *n*-octyldimethylchlorosilane ( $\text{C}_8\text{-Cl}$ ), *n*-octyldimethylhydroxysilane ( $\text{C}_8\text{-OH}$ ), *n*-octyldimethylmethoxysilane ( $\text{C}_8\text{-OCH}_3$ ), *n*-octyldimethylethoxysilane ( $\text{C}_8\text{-OC}_2\text{H}_5$ ), *n*-octyldimethyl(trifluoroacetoxy)silane ( $\text{C}_8\text{-OCOCF}_3$ ), and bis(*n*-octyldimethylsiloxane) ( $\text{C}_8\text{-O-C}_8$ ).

Three aspects are dealt with in detail, as follows:

(1) The mechanisms involved in the reaction of silica with  $\text{C}_8\text{-Cl}$ ,  $\text{C}_8\text{-OH}$  and  $\text{C}_8\text{-OCH}_3$ .

(2) The effect on the resulting ligand density caused by variation in the water content of the reactant solutions, the pretreatment temperature of the silica, and the reaction temperature.

(3) The tentative proposal of a relative reactivity scale for silanes, based on the experimental results obtained.

## EXPERIMENTAL

*Silanes*

*C<sub>8</sub>-Cl*. This material was prepared<sup>24,29</sup> by hydrosilylation of *n*-octene and dimethylchlorosilane by using hexachloroplatinic acid as catalyst (b.p. at 1860 Pa = 381 K; yield, 87%).

$C_8-OH$ . A solution of  $C_8-Cl$  in absolute diethyl ether was added dropwise to a stirred mixture of water (1 equiv.), freshly distilled aniline (1 equiv.) and absolute ether. The precipitated hydrochloride was removed and the filtrate was dried over sodium sulphate, and fractionally distilled. The purity of  $C_8-OH$  was determined by infrared spectroscopy and gas chromatography (b.p. at 13 Pa = 335–337 K; yield, 89%).

$C_8-OCH_3$ . A solution of  $C_8-Cl$  in excess methanol, containing one equivalent of triethylamine, was heated to reflux. The resulting hydrochloride was washed with chloroform, and the solvents were combined and subjected to fractional vacuum distillation (b.p. at 1066 Pa = 374 K; yield, 85%).

$C_8-OC_2H_5$ . This was prepared analogously to  $C_8-OCH_3$  (b.p. at 1466 Pa = 383 K; yield, 83%).

$C_8-N(CH_3)_2$ . Dry dimethylamine gas was passed through a solution of  $C_8-Cl$  in *n*-hexane. Dimethylamine hydrochloride was removed by filtration and the product was isolated by fractional distillation of the solution (b.p. at 1860 Pa = 392.5 K; yield, 88%).

$C_8-OCOCF_3$ . This material was synthesised according to the procedure of Corey *et al.*<sup>28</sup>. An equivalent amount of trifluoroacetic acid was added to  $C_8-Cl$ , and the desired product was isolated by fractional distillation (b.p. at 1160 Pa = 389 K; yield, 90%).

$C_8-O-C_8$ .  $C_8-Cl$  was hydrolysed with one equivalent of water in dry acetone and purified by fractional distillation (b.p. at 13 Pa = 408 K; yield, 97%).

All silanes were identified by IR (Jasco spectrometer) and  $^{13}C$  NMR (80 MHz, Bruker spectrometer) spectroscopy.

### Silica

The mesoporous silica from Grace (Worms, F.R.G.) used throughout had the following properties: specific surface area,  $a_s(\text{BET}) = 297 \pm 5 \text{ m}^2 \text{ g}^{-1}$ ; mean pore diameter,  $pd_{50} = 25 \text{ nm}$  (mercury intrusion); mean particle diameter,  $dp_{50} = 10 \mu\text{m}$  (Coulter counter).

The content of physically adsorbed water ( $\alpha_{H_2O}$ ) and the content of surface hydroxyl groups ( $\alpha_{OH(s)}$ ) were determined by the method of Holik and Matějková<sup>32</sup>, via exchange with deuterated trifluoroacetic acid (reagent grade, Merck) and subsequent  $^1H$  NMR (80 MHz, Bruker) spectroscopy. Samples were handled under dry nitrogen in a glove box, and the values of  $\alpha_{H_2O}$  and  $\alpha_{OH(s)}$  were measured as a function of the thermal pretreatment of the silica in the range 400–900 K (see Fig. 1).

### Surface modification

*Series 1.* Silica samples (2.5 g) were pretreated in separate containers at 373 K under vacuum at  $p \leq 13 \text{ Pa}$  for 18 h, and a set of solutions (dry dichloromethane, 50 ml) was prepared in parallel, each containing 2,4-lutidine (0.75 g) and defined amounts of water in the range 10–500 mg. After addition of  $C_8-Cl$  (1.32 g = 6.31 mmol) to each solution, these were immediately transferred to the corresponding silica by suction. The resulting suspensions were refluxed (313 K) for 4 h under gentle stirring. The silica was filtered off and washed successively with chloroform, ethanol, ethanol–water (1:1), and diethyl ether, then dried at 353 K under vacuum overnight. The amount of water in each solution was corrected with respect to the water contents

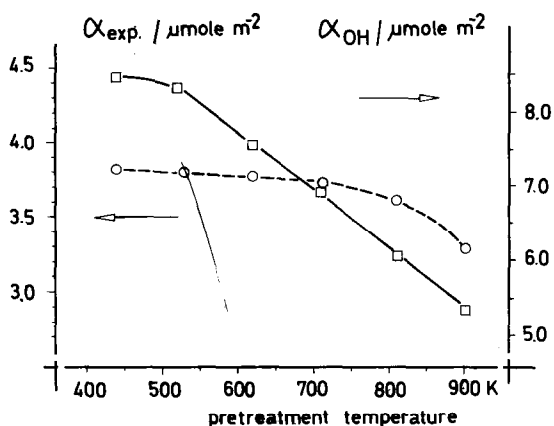


Fig. 1. Ligand density of *n*-octyldimethylsilyl groups,  $\alpha_{\text{exp}}$ , (○) and hydroxyl group concentration of native silica,  $\alpha_{\text{OH}}$ , (□) as a function of the pretreatment temperature (for conditions see series 2).

of the silica (3.5 mg), 2,4-lutidine (0.3 mg) and dichloromethane (2.0 mg). The  $\text{C}_8\text{-Cl}$  did not contain any detectable amount of water, as measured by the Karl Fischer test. Twelve preparations were carried out in two runs under identical conditions. In addition, a control experiment was carried out in duplicate, where the only water present in the preparation originated from the silica, lutidine, and dichloromethane in the amounts defined above.

**Series 2.** Silica samples (2.5 g) were pretreated for 24 h in separate containers at defined temperatures in the range 438–903 K under a vacuum of *ca.* 0.4 Pa, and then cooled to room temperature. Before the vacuum was released, each sample was separately treated with a solution of  $\text{C}_8\text{-N}(\text{CH}_3)_2$  (2.03 g = 9.47 mmol) in dry dichloromethane (50 ml). The resulting suspensions were refluxed (313 K) for 4 h under gentle stirring. The silica was filtered off and washed successively with chloroform, ethanol, ethanol–water (1:1), and diethyl ether, then dried at 353 K under vacuum overnight. Each preparation was duplicated.

**Series 3.** Silica samples (2.5 g) were pretreated at 373 K under vacuum. After cooling, these were then separately treated with solutions of the following silanes (9.48 mmol) in *N,N*-dimethylformamide (50 ml, reagent grade, Merck):  $\text{C}_8\text{-Cl}$ ,  $\text{C}_8\text{-OH}$ ,  $\text{C}_8\text{-OCH}_3$ ,  $\text{C}_8\text{-N}(\text{CH}_3)_2$ ,  $\text{C}_8\text{-O-C}_8$ , whereby 2,4-lutidine catalyst was added to the solutions of  $\text{C}_8\text{-Cl}$  (1.12 g = 10.4 mmol),  $\text{C}_8\text{-OH}$ ,  $\text{C}_8\text{-O-CH}_3$ , and  $\text{C}_8\text{-O-C}_8$  (each 0.101 g = 0.95 mmol). The solution of  $\text{C}_8\text{-N}(\text{CH}_3)_2$  was free of added base. The suspensions were then subjected to defined reaction temperatures in the range 274–426 K for 4 h. The preparations were repeated under identical conditions.

**Series 4.** Silica samples (2.5 g) were heated for 24 h in open ampoules (100 ml) at 373 K under vacuum. After cooling, each sample was treated with 47.4 mmol of one of the silanes in the absence of solvent, whereby for the following silanes an amount of the catalyst 2,4-lutidine was also added:  $\text{C}_8\text{-Cl}$  and  $\text{C}_8\text{-OCOCF}_3$  (0.51 g = 4.7 mmol);  $\text{C}_8\text{-Cl}$ ,  $\text{C}_8\text{-OCH}_3$ ,  $\text{C}_8\text{-OC}_2\text{H}_5$ , and  $\text{C}_8\text{-OH}$  (5.58 g = 51.7 mmol). The reagent  $\text{C}_8\text{-N}(\text{CH}_3)_2$  was used without added base. The ampoules were then sealed, and the reaction temperature was set to 313 K and 373 K in a parallel series of

preparations, in each case for 4 h. All preparations were also duplicated at each temperature. Successive washing and further workup was then carried out.

#### *Assessment of ligand density*

The ligand density ( $\alpha_{\text{exp}}$ ) of bonded *n*-octyldimethylsilyl groups was calculated from the carbon content of the modified sample, using the specific surface area [ $a_s(\text{BET}) = 297 \text{ m}^2 \text{ g}^{-1}$ ] corrected for the weight increase due to surface modification<sup>21,22</sup>. Applying the molar mass of *n*-octyldimethylsilyl [ $M_C$  (= molar mass of carbon in an *n*-octyldimethylsilyl group) =  $120.11 \text{ g mol}^{-1}$ ] and the bonded group ( $M_{\text{mod}} = 171.38 \text{ g mol}^{-1}$ ),  $\alpha_{\text{exp}}$  was obtained from the formula

$$\alpha_{\text{exp}} = \frac{P_C}{3\,567\,300 (1 - 0.01418 P_C)}$$

where  $P_C$  is the carbon content of the sample in weight percent.

#### *Chromatographic measurements*

Reversed-phase silica was packed into  $125 \times 4.6 \text{ mm}$  I.D. columns by the slurry technique, and tested by the procedure of Daldrup and Kardel<sup>33</sup> with an eluent consisting of acetonitrile (156 g) and phosphate buffer (pH 2.3) [total = 340 g; content 6.66 g/l potassium dihydrogenphosphate and 4.8 g/l phosphoric acid (85% w/w)], and with diphenhydramine (DPH), diazepam (DZP) and 5-(*p*-methylphenyl)-5-phenylhydantoin (MPPH) as test solutes. Detection was carried out at a wavelength of 220 nm. The chromatograph used was a Knauer Kompakt Anlage (Knauer, Bad Homburg, F.R.G.), fitted with a Hewlett-Packard integrator, Model 3385 A. A small amount of methanol was added to the eluent for marking  $t_m$ , the elution time of an unretained solute.

## RESULTS AND DISCUSSION

#### *Reaction of silica with C<sub>8</sub>-Cl*

Although the relative reactivity of monochlorosilanes is given by the series  $\text{R}_3\text{SiCl} < \text{R}_2\text{SiCl}_2 < \text{RSiCl}_3$  (in accordance with the rates of hydrolysis), they nevertheless possess an advantage over di- and trichlorosilanes in that the bonding to silica is limited to a one-bond mode in a well-defined stoichiometric relationship. The relatively low reactivity can be offset by using a stoichiometric excess of an amine, which functions as catalyst and base. On treatment of the activated silica (at room temperature) with increasing equivalent amounts of C<sub>8</sub>-Cl in xylene and using pyridine as base, it was established that the added silane was completely bound to the silica up to a surface concentration of *ca.*  $2.0 \mu\text{mol m}^{-2}$ . Higher ligand densities (up to a maximum of *ca.*  $3.5 \mu\text{mol m}^{-2}$ ) were achieved<sup>24</sup> by using a fourfold excess of silane at a temperature of 368 K. It has also been shown<sup>29</sup> that the type of base and the type of solvent both influence the reactivity of C<sub>8</sub>-Cl. Thus, the use of imidazole in dichloromethane gave a density of  $3.53 \mu\text{mol m}^{-2}$  at 323 K with an equivalent amount of C<sub>8</sub>-Cl. The observation that 2.0 out of a total of  $3.5 \mu\text{mol m}^{-2}$  surface hydroxyls reacted with C<sub>8</sub>-Cl at room temperature might be an indication that the former belong to especially reactive (*i.e.* free) hydroxyl groups.

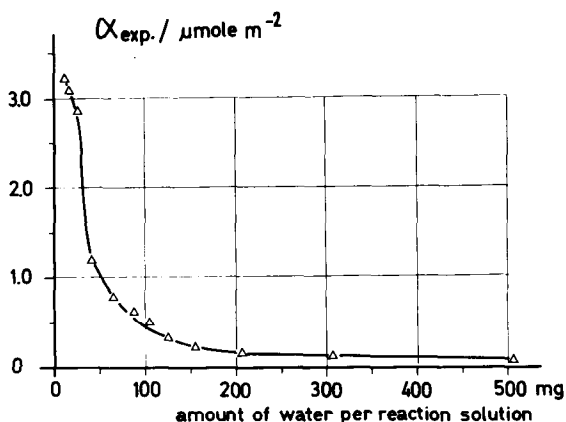


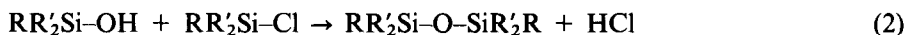
Fig. 2. Ligand density of *n*-octyldimethylsilyl groups on silica as a function of the water content of the starting reaction solution at silanisation (for conditions see series 1).

It has been claimed<sup>17</sup> that the modification of silica with monochlorosilanes is less sensitive to traces of water present in the reaction suspension, compared with modifications in which di- and trichlorosilanes are used. The results obtained in series 1 of the present study do not support this view. The data of Fig. 2 clearly indicate that the ligand density of bonded  $C_8$  groups falls dramatically when the water content in the reaction system is raised, while  $\alpha_{exp}$  remains essentially unaffected at water contents above 200 mg, and approaches a saturation value. There are two likely explanations for the course of this function, and these will be briefly discussed in turn.

In the first case, the water present reacts with  $C_8\text{-Cl}$ , yielding  $C_8\text{-OH}$ :



where  $R = n\text{-octyl}$  and  $R' = CH_3$ . This is followed by reaction of the  $C_8\text{-OH}$  with  $C_8\text{-Cl}$ , yielding  $C_8\text{-O-}C_8$ :



Reaction 2 is known to be acid-catalysed, and can be shown to proceed readily. Thus, in the present work, the rate of formation of disiloxane was monitored (by  $^{29}\text{Si}$  NMR spectroscopy) in a reaction conducted in the absence of silica, *i.e.* with an equimolar solution of  $C_8\text{-Cl}$  and  $C_8\text{-OH}$  in  $\text{CDCl}_3$ . The initial spectrum showed two peaks at 31.9 and 17.4 ppm, which were assigned to  $\text{Si-Cl}$  and  $\text{Si-OH}$ , respectively. Within 10 min of mixing, the intensity of these peaks diminished, and at 7.5 ppm a new peak appeared, which was assigned to the  $\text{Si-O-Si}$  resonance.

In the case of reaction 1, the amount of water necessary to convert one half of the  $C_8\text{-Cl}$  into  $C_8\text{-OH}$  in the presence of suspended silica can be easily derived from the starting amounts of reactants: for an initial 6.31 mmol of  $C_8\text{-Cl}$  the amount of water is 3.16 mmol (57 mg). The remaining half of the  $C_8\text{-Cl}$  then reacts further with  $C_8\text{-OH}$ , yielding  $C_8\text{-O-}C_8$ , according to reaction 2. Thus, increasing amounts

TABLE I  
CHEMICAL SHIFTS OF SILICON IN SILANES BY  $^{29}\text{Si}$  NMR

Silane	$\delta_{\text{silane}}$ (ppm)	$\delta_{\text{silane} + 2,4\text{-lutidine}}$ (ppm)
$\text{C}_8\text{-OH}$	17.61	11.40
$\text{C}_8\text{-OCH}_3$	19.63	18.22
$\text{C}_8\text{-Cl}$	31.85	31.08

of water (up to *ca.* 60 mg) will convert  $\text{C}_8\text{-Cl}$  into the less reactive  $\text{C}_8\text{-O-C}_8$ , and a sharp drop in  $\alpha_{\text{exp}}$  in this water range may be rationally accounted for.

The second case to be considered involves rapid adsorption of the water present in the solution onto the silica surface on generation of the suspension. Applying the cross-sectional area of the water molecule ( $a_m = 0.2 \text{ nm}^2/\text{H}_2\text{O}$ ), the monolayer capacity of adsorbed water can be deduced to be  $8.33 \mu\text{mol m}^{-2}$ . This value, combined with  $a_s(\text{BET}) = 297 \text{ m}^2 \text{ g}^{-1}$  and the starting weight of the active silica (2.5 g), leads to a computed 114.3 mg of water adsorbed at the surface. This exactly equals the amount required for the total hydrolysis of  $\text{C}_8\text{-Cl}$  to  $\text{C}_8\text{-OH}$ . Thus, the results could also be accounted for by assuming that a monolayer of water inhibits the direct attack of  $\text{C}_8\text{-Cl}$  at a surface hydroxyl, leading rather to the formation of  $\text{C}_8\text{-OH}$  as an intermediate, which in turn is less reactive towards the surface hydroxyls than is  $\text{C}_8\text{-Cl}$  itself.

In the absence of detectable amounts of water, the  $\text{C}_8\text{-Cl}$  is assumed to react directly with the hydroxyl groups of the silica via a reactive intermediate containing an  $\text{Si-N}^+$  bond, arising from the reaction of  $\text{C}_8\text{-Cl}$  with 2,4-lutidine. The interaction of 2,4-lutidine with the silanes  $\text{C}_8\text{-Cl}$ ,  $\text{C}_8\text{-OCH}_3$ , and  $\text{C}_8\text{-OH}$  was also monitored by  $^{29}\text{Si}$  NMR spectroscopy. The addition of 2,4-lutidine to solutions of  $\text{C}_8\text{-Cl}$ ,  $\text{C}_8\text{-OCH}_3$ , and  $\text{C}_8\text{-OH}$  produced a shift of the silicon resonance to a higher field value than that observed for the pure silane solution, as listed in Table I.

For comparison, the chemical shift of  $\text{C}_8\text{-N}(\text{CH}_3)_2$  is 8.40 ppm. Since the reaction between the base and the silane is reversible and fast, no pure shifts for a silicon-lutidine complex can be isolated from the data in the above table; the values in the third column refer to a mean chemical shift given by

$$\delta = c_X \delta_{\equiv\text{Si-X}} + c_N \delta_{\equiv\text{Si-N=}}$$

The chemical shifts of the three compounds are seen to decrease in the sequence  $\text{C}_8\text{-OH} \gg \text{C}_8\text{-OCH}_3 > \text{C}_8\text{-Cl}$ . A possible explanation is that the extent of the shift reflects the stability of the intermediate, *i.e.* stronger interactions produce larger shifts; it would then appear certain that a stable intermediate state also exhibits a lower reactivity, and hence the shift variations remain in accord with the reactivity of the silanes.

It was established that no change in chemical shift took place when silica was added to the pure silane. These experiments clearly support the catalytic involvement of the lutidine in addition to its obvious function as a base.

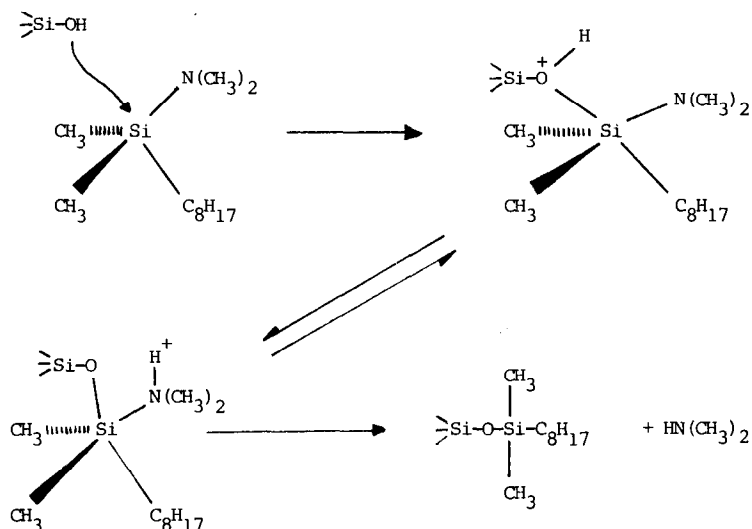
#### Reaction of silica with $\text{C}_8\text{-OH}$

The reaction of *n*-alkyldimethylhydroxysilanes and *n*-oxaalkyldimethylhydrox-





atisation of hydroxyl functions in gas chromatography<sup>37</sup>. The reaction of trialkyldimethylaminosilanes on Cab-O-Sil and Aerosil has been studied in detail<sup>26,27,38</sup>. The intrinsic high reactivities of the silanes resulted in limiting ligand densities of  $4.75 \mu\text{mol m}^{-2}$  for trimethylsilyl groups<sup>38</sup>, whereas  $4.1 \mu\text{mol m}^{-2}$  was achieved for longer chain lengths<sup>27</sup>. The following mechanism was proposed for the reaction of  $\text{C}_8\text{-N}(\text{CH}_3)_2$  with silica:



The nucleophilic silica hydroxyl attacks the silicon of the organosilane, forming a pentavalent transition-state adduct. This state is in equilibrium with a second, in which the proton has migrated to the amine nitrogen. Release of dimethylamine gives the final product.

Thus, the reactions of  $\text{C}_8\text{-Cl}$  and  $\text{C}_8\text{-N}(\text{CH}_3)_2$  differ mainly in that  $\text{C}_8\text{-N}(\text{CH}_3)_2$  already contains a reactive Si-N bond, whereas this bond must first be generated by the intervention of an amine catalyst in the case of  $\text{C}_8\text{-Cl}$ . A second difference lies in the fact that the co-product dimethylamine is very volatile in the one case, whereas with  $\text{C}_8\text{-Cl}$  a salt is formed.

In series 2 the effect of the pretreatment temperature of the silica on the ligand density was studied. Fig. 1 summarizes the results. It is apparent that the hydroxyl group concentration at an activation temperature of 450 K reaches  $8.5 \mu\text{mol m}^{-2}$  and then falls linearly with increasing calcination. Even at 900 K a remarkably high value of  $\alpha_{\text{OH(s)}}$  is still evident. In contrast to this dependency, the ligand density of bonded  $\text{C}_8$  groups on these pretreated silicas falls only slightly with increase in the pretreatment temperature up to 800 K. This is in accord with the assumption that highly reactive (*i.e.* isolated) hydroxyl groups are the reactive surface sites, and these are not involved in dehydroxylation processes until the pretreatment temperature rises above 800 K.

#### Reaction of silica with $\text{C}_8\text{-OCOCF}_3$

Corey *et al.* adapted this reaction to the synthesis of *n*-octadecylsilica pack-

ings<sup>28</sup>. In a comparative study between trialkyltrifluoroacetoxysilanes and trialkylchlorosilanes, Kinkel and Unger<sup>29</sup> found no significant differences in the ligand densities, a result that was confirmed by the results of the present examination.

#### Reaction of silica with C<sub>8</sub>-O-C<sub>8</sub>

A previous paper<sup>39</sup> has described the reaction of *n*-hexyltetramethyldisiloxane (DHTMDO) and di-*n*-hexyl(tetramethyl)disilazane (DHTMDS) with LiChrosorb Si 100 (Merck) at 623 K in the absence of solvent. The resulting ligand densities were 2.3 (DHTMDO) and 3.7  $\mu\text{mol m}^{-2}$  (DHTMDS). Boksányi *et al.*<sup>35</sup> have reported on the reaction of hexamethyldisiloxane (HMDSO) with Cab-O-Sil at 523 and 573 K. In this case, after a 24-h reaction, the ligand densities were 2.81 and 3.09  $\mu\text{mol m}^{-2}$ , respectively. It can be concluded that even the smallest disiloxane (HMDSO) is less reactive in silanisation and requires high temperatures to become activated. This is in accord with our findings. On a silica activated at 373 K, the treatment with C<sub>8</sub>-O-C<sub>8</sub> in the presence of 2,4-lutidine at 353 K gave a ligand density of 0.72  $\mu\text{mol m}^{-2}$  after 4 h, which is the lowest value of all the silanes studied in this series (series 4).

#### Comparison of the reactivity of silanes under standardised conditions

To achieve a reliable comparison of the reactivity of silanes, the reaction was carried out under standardised conditions in two sets of experiments.

In series 3, the reactivity of silanes was examined in the presence of 2,4-lutidine in *N,N*-dimethylformamide in the temperature range 274–426 K. The results are shown in Fig. 3 in the form of a plot of  $\alpha_{\text{exp}}$  vs. the reaction temperature for each silane studied. Very distinct dependencies can be observed. It is worth noting that the silanisation reactions were carried out in open systems, in contrast to series 4, where closed ampoules were used. In this way, the volatile co-products (dimethylamine, water and methanol) readily evolve. The most reactive silane of this study [C<sub>8</sub>-N(CH<sub>3</sub>)<sub>2</sub>] yielded a ligand density of 2.5  $\mu\text{mol m}^{-2}$ , even at 274 K. However, above this temperature the conversion curve flattens off and approaches a saturation value. The limit of 4.1  $\mu\text{mol m}^{-2}$  is in close agreement with the values reported for Cab-

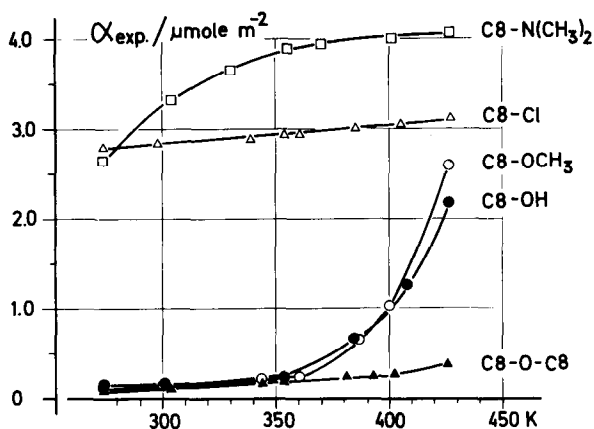


Fig. 3. Ligand density of *n*-octyldimethylsilyl groups on silica as a function of the reaction temperature for different silanes (for conditions see series 3).

O-Sil and Aerosil<sup>27</sup>. The high conversion at relatively low temperatures is probably favoured by the high volatility of the co-product dimethylamine. A similar situation was found in the modification of silica with C<sub>8</sub>-enolate; acetylacetone was formed and easily removed under the high-vacuum conditions employed<sup>31</sup>.

Surprisingly, the ligand density reached by C<sub>8</sub>-Cl at 275 K is slightly higher than that of C<sub>8</sub>-N(CH<sub>3</sub>)<sub>2</sub>. A slight linear increase with rising temperature is observed for C<sub>8</sub>-Cl, with a slope similar to that for C<sub>8</sub>-O-C<sub>8</sub>. The hydrochloride formed is quickly bound to the base 2,4-lutidine, the hydrochloride of which is soluble in dimethylformamide. It is known that the formation of the hydrochloride is slightly temperature-dependent, and this could account for the small slope of the function. In the case of the disiloxane, the extremely low reactivity seems to control the reaction dependence, whereby a notable conversion can be expected only at much higher temperatures and, furthermore, in the absence of solvent. The graphs for C<sub>8</sub>-OH and C<sub>8</sub>-OCH<sub>3</sub> have essentially identical forms, whereby the initial part of the curve is characterised by an extremely low conversion, corresponding to the low reactivity of these silanes. However, above 390 K a linear increase of  $\alpha_{exp}$  with increasing temperature becomes evident, which is probably due to evaporation of the volatile co-products from the pore system, which shifts the equilibrium to the product side. Unfortunately, higher reaction temperatures could not be employed (solvent limitation); otherwise, these curves might have been expected to flatten out to a saturation value of *ca.* 4  $\mu\text{mol m}^{-2}$ .

In series 4, all the silanes were made to react with the silica in a closed system in the absence of solvent. The experiments were carried out at 313 and 353 K. Table II shows the ligand densities achieved. The reactivity follows the sequence: C<sub>8</sub>-N(CH<sub>3</sub>)<sub>2</sub> > C<sub>8</sub>-OCOCF<sub>3</sub> > C<sub>8</sub>-Cl  $\gg$  C<sub>8</sub>-OR  $\gg$  C<sub>8</sub>-O-C<sub>8</sub> where R = H, CH<sub>3</sub>, or C<sub>2</sub>H<sub>5</sub>.

By far the most reactive silanes were C<sub>8</sub>-N(CH<sub>3</sub>)<sub>2</sub>, C<sub>8</sub>-OCOCF<sub>3</sub>, and C<sub>8</sub>-Cl. The second group, with considerably lower values of  $\alpha_{exp}$ , consists of C<sub>8</sub>-OH, C<sub>8</sub>-OCH<sub>3</sub>, and C<sub>8</sub>-OC<sub>2</sub>H<sub>5</sub>. The reagent C<sub>8</sub>-O-C<sub>8</sub> provided the lowest ligand density. It is worth comparing the results with those obtained with other reactive silanes, *e.g.* *n*-octyl enolate, as described by Bien-Vogelsang *et al.*<sup>31</sup>. On Nucleosil 5-100, a ligand

TABLE II  
LIGAND DENSITIES OF BONDED *n*-OCTYLDIMETHYLSILYL GROUPS

Densities quoted at two reaction temperatures, resulting from the reaction of a 25-nm pore-size silica with seven different silanes (for conditions see *Series 4*).

Silane	$\alpha_{exp}$ ( $\mu\text{mol m}^{-2}$ )	
	313 K	353 K
C <sub>8</sub> -O-C <sub>8</sub>	0.47 $\pm$ 0.13	0.72 $\pm$ 0.13
C <sub>8</sub> -OC <sub>2</sub> H <sub>5</sub>	1.22	2.39
C <sub>8</sub> -OCH <sub>3</sub>	1.38	2.55
C <sub>8</sub> -OH	1.40	2.55
C <sub>8</sub> -Cl	3.41	3.57
C <sub>8</sub> -OCOCF <sub>3</sub>	3.76	3.80
C <sub>8</sub> -N(CH <sub>3</sub> ) <sub>2</sub>	3.78	4.10

density of  $3.7 \mu\text{mol m}^{-2}$  was achieved (see Table VI of Ref. 31) at a reaction temperature of 303 K after 4 h. A comparison of the  $\alpha_{\text{exp}}$  values obtained for the four reactive silanes [ $\text{C}_8\text{-enolate}$ ,  $\text{C}_8\text{-N}(\text{CH}_3)_2$ ,  $\text{C}_8\text{-OCOFC}_3$ ,  $\text{C}_8\text{-Cl}$ ] shows them scattered around an average of  $3.8 \pm 0.3 \mu\text{mol m}^{-2}$ , the differences being relatively insignificant. The reproducibility of ligand densities was similar to that found in the present study, namely *ca.*  $\pm 0.1 \mu\text{mol m}^{-2}$  under carefully standardised conditions.

Significant factors in the choice of a silane with regard to economic manufacture of *n*-octyl reversed-phase packings are the cost of the silane per unit mass of silica, and the labour costs related to the modification. The cheapest silane of the four mentioned above is the monochlorosilane, this having a current price of *ca.* US\$150 per kg in the F.R.G. All three remaining silanes are more expensive, since the monochlorosilane is used as a starting material for each, and must be converted by a consecutive reaction into the corresponding products. Costs related to the pre-treatment (*e.g.* vacuum, reaction temperature, excess amount of silane, etc.) must also be taken into account.

From the point of view of chromatographic performance, the retention and selectivity of these reversed-phase packings were found to be determined solely by the ligand density, and were independent of the type of silane employed in the manufacture. A linear relationship was established for the plot of capacity factor of test solutes against ligand density of the packing at an eluent pH of 2.3. Naturally, the validity of this statement assumes a constant silica as starting material and a constant test procedure.

## REFERENCES

- 1 R. E. Majors and H. J. Hopper, *J. Chromatogr. Sci.*, 12 (1974) 767.
- 2 R. K. Gilpin, J. A. Korpi and C. A. Janicki, *Anal. Chem.*, 46 (1974) 1314.
- 3 J. H. Knox and A. Pryde, *J. Chromatogr.*, 112 (1975) 171.
- 4 J. J. Kirkland, *Chromatographia*, 8 (1975) 661.
- 5 D. G. I. Kingston and B. B. Gerhart, *J. Chromatogr.*, 116 (1976) 182.
- 6 E. J. Kikta and E. Grushka, *Anal. Chem.*, 48 (1976) 1098.
- 7 K. Karch, I. Sebastian and I. Halász, *J. Chromatogr.*, 122 (1976) 3.
- 8 H. Hemetsberger, W. Maasfeld and H. Ricken, *Chromatographia*, 9 (1976) 303.
- 9 H. Hemetsberger, M. Kellermann and H. Ricken, *Chromatographia*, 10 (1977) 726.
- 10 C. J. Little, A. D. Dale and M. B. Evans, *J. Chromatogr.*, 153 (1978) 381, 543.
- 11 M. C. Hennion, C. Picard and M. Caude, *J. Chromatogr.*, 166 (1978) 21.
- 12 C. J. Little, A. D. Dale, J. B. Whatley and M. B. Evans, *J. Chromatogr.*, 171 (1979) 431.
- 13 C. J. Little, J. A. Whatley, A. D. Dale and M. B. Evans, *J. Chromatogr.*, 171 (1979) 435.
- 14 H. Hemetsberger, P. Behrensmeier, J. Henning and H. Ricken, *Chromatographia*, 12 (1979) 71.
- 15 M. B. Evans, A. D. Dale and C. J. Little, *Chromatographia*, 13 (1980) 5.
- 16 H. Engelhardt and G. Ahr, *Chromatographia*, 14 (1981) 227.
- 17 H. Engelhardt, B. Dreyer and H. Schmidt, *Chromatographia*, 16 (1982) 11.
- 18 C. Dewaele, P. Mussche and M. Verzele, *J. High Resolut. Chromatogr. Chromatogr. Commun.*, 5 (1982) 616.
- 19 M. Verzele and P. Mussche, *J. Chromatogr.*, 254 (1983) 117.
- 20 E. Bayer, K. Albert, J. Reiners, M. Nieder and D. Müller, *J. Chromatogr.*, 264 (1983) 197.
- 21 K. K. Unger, N. Becker and P. Roumeliotis, *J. Chromatogr.*, 125 (1976) 115.
- 22 P. Roumeliotis and K. K. Unger, *J. Chromatogr.*, 149 (1978) 211.
- 23 G. E. Berendsen and L. de Galan, *J. Liq. Chromatogr.*, 1 (1978) 403; 561.
- 24 G. E. Berendsen, K. A. Pikaart and L. de Galan, *J. Liq. Chromatogr.*, 3 (1980) 1437.
- 25 N. Tanaka, H. Goodell and B. L. Karger, *J. Chromatogr.*, 158 (1978) 233.
- 26 E. Kováts, sz., *Ger. Pat.*, 2.930.516 (1979).

- 27 J. F. Erard, L. Nagy and E. Kováts, sz., *Colloids Surfaces*, 9 (1984) 109.
- 28 E. J. Corey, H. Cho, Ch. Rückler and D. H. Hua, *Tetrahedron Lett.*, 22 (1981) 3455.
- 29 J. N. Kinkel and K. K. Unger, *J. Chromatogr.*, 316 (1984) 193.
- 30 G. Schomburg, A. Deege, J. Köhler and U. Bien-Vogelsang, *J. Chromatogr.*, 282 (1983) 27.
- 31 U. Bien-Vogelsang, A. Deege, H. Figge, J. Köhler and G. Schomburg, *Chromatographia*, 19 (1984) 170.
- 32 M. Holik and B. Matějková, *J. Chromatogr.*, 213 (1981) 33.
- 33 T. Daldrup and B. Kardel, *Chromatographia*, 18 (1984) 81.
- 34 K. K. Unger, *Porous Silica*, Elsevier, Amsterdam, 1979, pp. 57–67.
- 35 L. Boksányi, O. Liardon, E. Kováts, sz., *Adv. Colloid Interface Sci.*, 6 (1976) 95.
- 36 H. Engelhardt and D. Mathes, *J. Chromatogr.*, 142 (1977) 311.
- 37 C. F. Poole and Sh. A. Schuette, *Contemporary Practice of Chromatography*, Elsevier, Amsterdam, 1984, pp. 485–496.
- 38 J. Gobet and E. Kováts, sz., *Adsorption Sci. Technol.*, 1 (1984) 77.
- 39 T. Welsch and H. Frank, *J. Chromatogr.*, 267 (1983) 39.