Facile Cleavage of Si−C Bonds during the Sol-Gel Hydrolysis of Aminomethyltrialkoxysilanes − A New Method for the Methylation of Primary Amines

Augustin Adima,[a] Catherine Bied,[a] Joël J. E Moreau,*[a] and Michel Wong Chi Man[a]

Keywords: Alkylation / Amines / Condensation / Hydrolysis / Sol-gel processes

The reaction of chloromethyltriethoxysilane with (1*R*,2*R*)-bis(methylamino)cyclohexane (**1**) afforded the corresponding bis-silylated compound **2**. The sol-gel hydrolysis of **2** did not give the expected bridged silsesquioxane owing to quantitative Si–C-bond cleavage. Instead, silica and (1*R*,2*R*)-bis(dimethylamino)cyclohexane (**3**) were obtained. This reaction was exploited to propose a new route for the methylation of amines. Such methylation reaction of amines could be extended to other amines and provides a new method for the selective monomethylation of primary amines.

Introduction

The sol-gel hydrolysis-condensation of organoalkoxysilanes has until now been used as a smooth method to achieve hybrid silicas.[1] In this context, multifunctional organosilanes with bridging organic units, $(RO)_3Si-R'-Si(OR)_3$, (R′ = organic bridging unit, R = Me, Et) were rapidly revealed to be interesting precursors to afford a new type of hybrid materials known as bridged silsesquioxanes.[2,3] This interesting route allows a high loading of organic fragments in silicas and materials chemists soon realized the importance of this molecular approach for the design of new materials. A wide variety of organosilylated compounds have led to materials with targeted properties.[4] Recently we reported the transcription of the chiral properties of the organic moiety to the hybrid material with the formation of right- and left-handed helical fibers.[5] The use of bridging organic units capable of self-association by hydrogen bonding allowed the formation of supramolecular assemblies and afforded a general method for the nanostructuration and the shaping of hybrid silicas.[6] We have already succeeded in the immobilization of chiral *trans*-(1*R*,2*R*)-diaminocyclohexane derivatives in a silica network.[7] The formation of [(1*R*,2*R*)-bis(triethoxysilylpropylamino)cyclohexyl]rhodium complexes, followed by sol-gel hydrolysis, gave a catalytic hybrid material which proved to be an efficient enantioselective catalyst for the asymmetric reduction of prochiral ketones. In an effort to improve the efficiency of these novel heterogeneous catalysts, we examined the possibility of synthesizing a related material from (1*R*,2*R*)-bis[methyl(triethoxysilylmethyl)amino]cyclohexane (**2**) with only one carbon alkylene spacer between the nitrogen and the silicon atoms. The replacement of the propylene by a methylene spacer was expected to enhance the rigidity of the hybrid chiral network and thereby induce better selectivity properties to the asymmetric catalytic material. Unexpectedly, during the hydrolysis-condensation step, significant cleavage of the Si−C bonds occurred, leading to the formation of silica (SiO_2) and leaching of (1*R*,2*R*)-bis(dimethylamino)cyclohexane (**3**). We report here our studies on the scope of this cleavage reaction and its possible use in the synthesis of methylated amines.

Results and Discussion

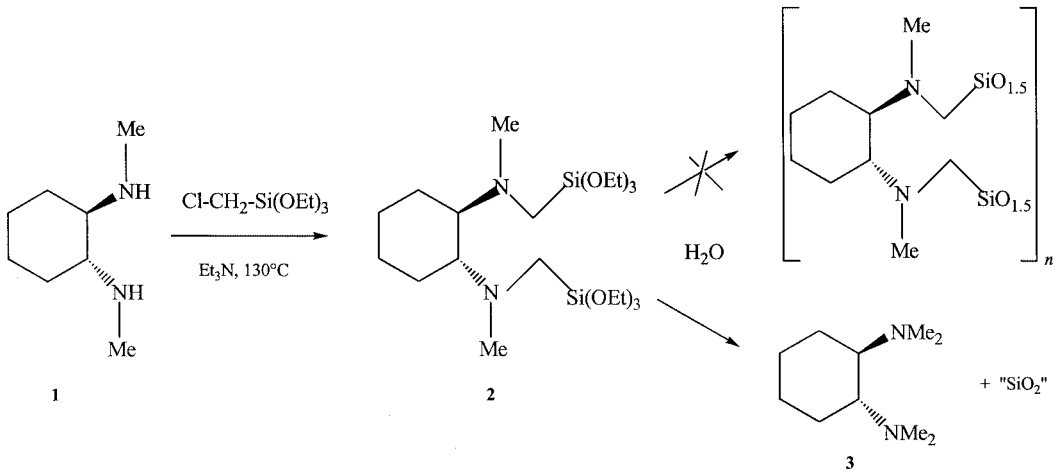
Synthesis and Hydrolysis of (1*R*,2*R*)-Bis[methyl(triethoxysilylmethyl)amino]cyclohexane (2)

The bis-silylated compound **2** was obtained in 68% yield by the reaction of an excess of chloromethyltriethoxysilane (3 molar equivalents) with (1*R*,2*R*)-bis(methylamino)cyclohexane (**1**; Scheme 1).[8] The hydrolysis-condensation of solutions of **2** was carried out in ethanol at room temperature with NH_4F as catalyst (0.1 mol %). A gel formed within one minute and then solubilized after one day, leading to a new solution. Then, a second gelation occurred within three days affording a stable gel. After aging for one week it was crushed and the resulting powder was washed with diethyl ether and dried under vacuum for one day at 60 °C.

This solid material was analyzed by FT-IR and ^{13}C and ^{29}Si solid-state NMR spectroscopy, and elemental analysis.

[a] Laboratoire de Chimie Organométallique, Hétérochimie Moléculaire et Macromoléculaire, UMR CNRS 5076, Ecole Nationale Supérieure de Chimie de Montpellier,
8, rue de l'Ecole Normale, 34296 Montpellier Cedex 05, France
Fax: +33-4- 67147212
E-mail: jmoreau@cit.enscm.fr

  DOI: 10.1002/ejoc.200400079



Scheme 1. Preparation and hydrolysis of the bis-silylated molecule **2**

Unexpectedly, the ^{29}Si NMR spectrum of this solid predominantly exhibits signals characteristic of SiO_4 substructures (Q^3 and Q^4) at $\delta = -100$ and -109 ppm, respectively, and only a low intensity signal centered at $\delta = -71$ ppm can be assigned to the expected $CSiO_3$ (T^3) substructures (Figure 1).

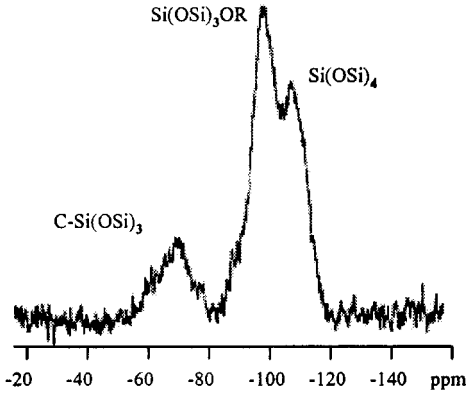


Figure 1. Solid state ^{29}Si NMR spectrum of solid material obtained upon hydrolysis of **2**

The presence of these Q units indicates a high amount of Si−C cleavage during the hydrolysis-condensation process,[3a] whereas the T^3 unit represents some residual organic fragments still covalently bonded to silicon. From this observation a significant loss of organics is expected. This loss was confirmed by elemental analysis of the dried gel, which gave an N to Si ratio of 0.33 instead of the ratio of 1 expected in the absence of Si−C cleavage.

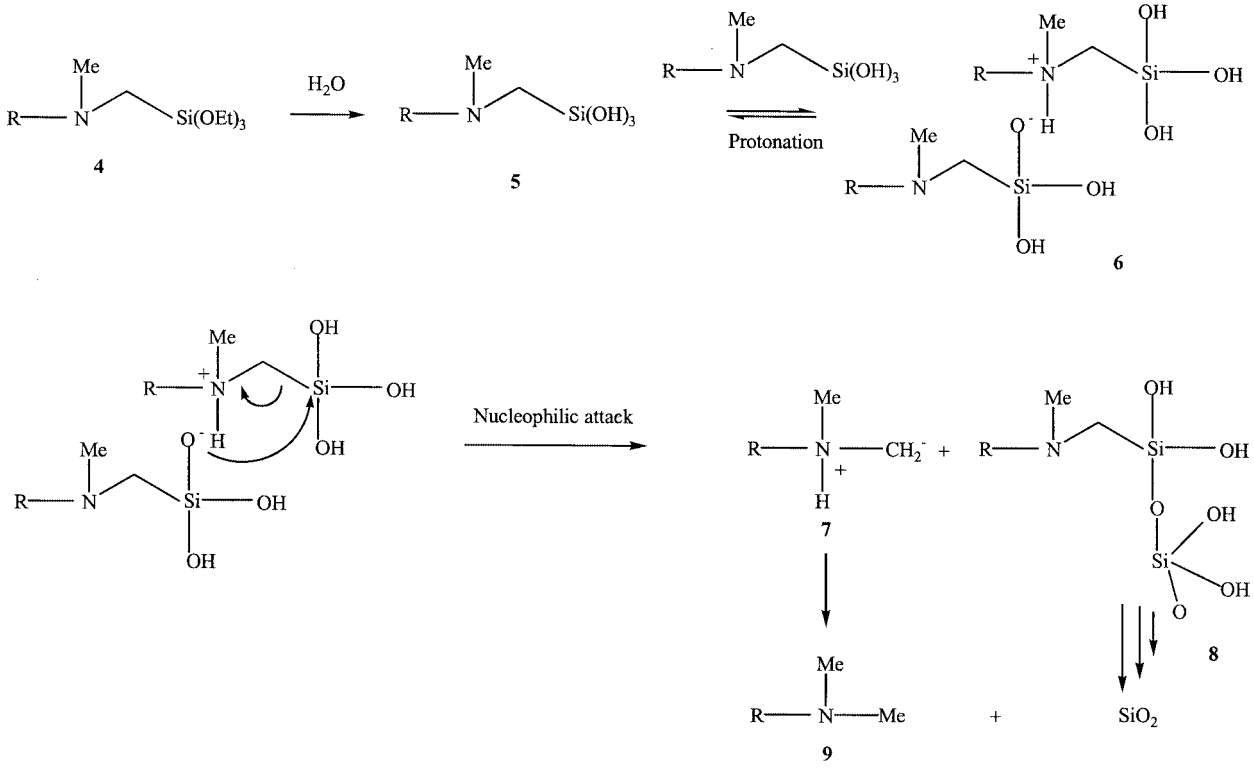
For a better understanding of this phenomenon, we decided to recover the organic compound formed during the hydrolysis process. The hybrid material was washed several times with diethyl ether and the solvents were evaporated from the filtrate. The ^1H and ^{13}C NMR spectra of the crude residue proved that the compound formed was actually (1*R*,2*R*)-bis(dimethylamino)cyclohexane (**3**). It should be noted that the Si−C bond cleavage only occurs in the presence of water and that it was not observed in dry EtOH. A related Si−C bond cleavage has already been observed in analogous phosphorus compounds in the presence of protic solvents such as MeOH or H_2O;[9] it is thought to involve a nucleophilic attack of the oxygen atom at silicon. Moreover, in the case of the quaternary silylammonium salt $Ph_3Si-CH_2N^+(CH_3)_2(CH_2Ph)$, Sato et al.[10] have also described the nucleophilic attack of the hydride ion on the Si−C bond of the ammonium ion leading to the cleavage of this bond and formation of Ph_3SiH.

From these results it seems that the reaction may proceed according to the following mechanism (Scheme 2). The hydrolysis of the (aminomethyl)trialkoxysilane **4** affords the silanol **5**. Due to the acidity of the silanol groups, a quaternary ammonium salt **6** forms. Related zwitterionic organosilicates of the type $RMe_2NCH_2SiF_4$ or $R_2N-(CH_2)_n-Si(OR)_4$ (n = 1, 3) stable in dry media have already been reported.[11] A nucleophilic attack of $Si-O^-$ at the silicon atom of the ammonium salt then leads to the cleavage of the Si−C bond with formation of the ammonium ylide **7** and a siloxane-bridged compound **8**. The rapid isomerization of **7** gives the dimethylamine **9**.

The occurrence of such a reaction during the hydrolysis of **2** prevents the preparation of a hybrid material by a sol-gel process as it selectively leads to the methylated amino derivative **3**. Therefore, we decided to explore the scope of this reaction leading to methylated amines from silylated precursors as it may be of interest for the selective preparation of monomethylated amines, especially because silica is the only by-product of this reaction. We examined the influence of several factors on the hydrolysis of aminomethylsilanes and then explored some use of the reaction for the methylation of primary amines.

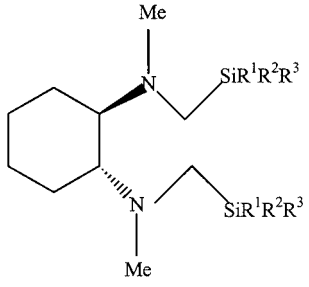
Influence of the Substituents at Silicon and of the Structure of the Amine

We first studied the influence of the number of alkoxy groups linked to the silicon atom on the rate of the Si−C bond cleavage. For this purpose, we prepared two diaminocyclohexane derivatives **10** and **11** (Scheme 3) and com-



Scheme 2. Mechanism of the Si−C bond cleavage by hydrolysis of (aminomethyl)silanes

pared their reactivity upon hydrolysis with that of compound **2** (Table 1). Compounds **10** and **11** were prepared following the same method used for the preparation of **2**.



2 : $R^1 = R^2 = R^3 = OEt$
10 : $R^1 = R^2 = R^3 = Me$
11 : $R^1 = R^2 = Me$, $R^3 = OEt$

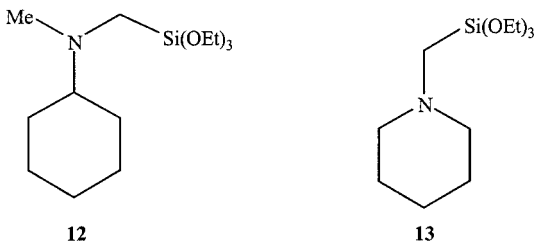
Scheme 3. Influence of the substituents at silicon on the hydrolysis of (aminomethyl)silanes

Table 1. Hydrolysis of amines **2**, **10, 11, 12** and **13**

Compound	Temperature	Reaction time (d)	Conversion (%)
2	20 °C	3	85
10	120 °C	2	10
11	20 °C	3	28
12	20 °C	3	52
13	20 °C	3	26

The hydrolysis reaction was performed on these three derivatives at room temperature in the presence of three equivalents of H_2O with EtOH as solvent and the reaction was monitored by ^1H NMR spectroscopy. In the case of compound **10**, bearing three CH_3 substituents at the silicon atom, no Si−C bond cleavage occurred at room temperature. After heating for two days at 120 °C, only 10% of compound **3** was obtained. When a methyl group was replaced by an ethoxy group (compound **11**), a conversion rate of 28% was observed after three days of reaction at room temperature, whereas in the case of the compound **2**, with three ethoxy groups at silicon, the reaction proceeded more rapidly (85% conversion under the same conditions). These results demonstrate that the number of ethoxy groups at silicon greatly influences the rate of the Si−C bond-cleavage: a faster reaction occurs when the electrophilicity of the Si atom is enhanced.

We then studied the influence of the structure of the amine on the reaction. We prepared the two derivatives **12** and **13** (Scheme 4) and performed their hydrolysis under the same conditions as those previously used for **2**.



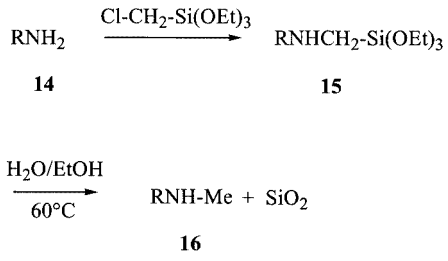
Scheme 4. Structures of the silylated amines **12** and **13**

The reactions were followed by ^{1}H NMR spectroscopy. This study shows that the reaction goes faster for the bis-silylated compound **2** than for **12** or **13** (Table 1). For the amine **13**, the steric hindrance may explain the low amount of Si−C cleavage during the hydrolysis of this compound.

Selective Monomethylation of Primary Amines

We finally explored whether this reaction could lead to selective monomethylation of primary amines. Various methods for the monomethylation of primary amines have been described in the literature,[12] but they often give poor yields and selectivities leading to polyalkylations. We therefore studied the application of the sol-gel hydrolysis of (aminomethyl)triethoxysilanes in organic synthesis, particularly for the methylation of primary amines using (chloromethyl)-triethoxysilane. The main advantages of this reaction are that it may be performed under mild conditions (low temperature and water as reactant) and it gives only silica as by-product, which can easily be removed by filtration.

To explore the scope of this new route, we used the following primary amines: diaminocyclohexane, aminocyclohexane, benzylamine, aniline and an amino ester (Phe-Ala-OMe). These amines **14** were first treated with chloromethyltriethoxysilane and then hydrolyzed to the corresponding methylated amines **16** (Scheme 5). The yields obtained are given in Table 2.



Scheme 5. Methylation of primary amines **14** via (aminomethyl)triethoxysilanes **15**

Table 2. Preparation of monomethylated amines **16** via (aminomethyl)triethoxysilanes **15**

14 a-e	15 a-e	16 a-e	Isolated yield (two-steps reaction)	Isolated yield[a] (one-pot reaction)
a-R = 	65%	98%	64%	-
b-R = 	-	-	-	68%
c-R = $PhCH_2$-	71%	84%	60%	-
d-R = Ph-	80%	63%	50%	80%
e-R = $PhCH_2C(H)CO_2Me$	67%	70%	47%	88%

[a] Without isolation of the silylated intermediate **15**.

We first carried out the reactions in two steps, isolating the (triethoxysilyl)methylamine intermediates **15**, which were then hydrolyzed in a second step to afford the monomethylamines **16**, leading to overall yields of between 47 and 64%. In the case of diaminocyclohexane (**14a**) a mixture of the mono- (**15a**) and the bis-silylated compounds was obtained; **15a** could be separated from the bis-silylated compound by distillation.[7a,7c]

Taking into account that the silica by-product can easily be removed by simple filtration, the direct one-pot syntheses of the methylated compounds **16b**, **16d** and **16e**, without isolation of the corresponding intermediates **15b**, **15d** and **15e**, was performed. In the case of the amines **14d** and **14e**, the yields were significantly improved to 80% in the case of aniline and 88% for the amino ester instead of 50% and 47% overall yields, respectively (Table 2). When benzylamine (**14c**) was used as substrate, the one-pot reaction gave a mixture of compounds: the expected monomethylbenzylamine, dimethylbenzylamine and *ortho*-methylbenzylamine; the latter results from a rearrangement of the silylated intermediate as already reported in the case of benzyl trialkylammonium salts.[13]

Compared to the other methods usually used for the methylation of amines, the procedure we describe here allows the selective preparation, under mild conditions, of the monomethylated derivative and avoids the formation of polymethylated products.[12] This selectivity is due to the use of (chloromethyl)triethoxysilane as a bulky methylating agent.

Conclusion

The bis-silylation of (1*R*,2*R*)-bis(methylamino)cyclohexane has been achieved by the reaction with (chloromethyl)-triethoxysilane. The hydrolysis of this compound did not give the expected bridged silsesquioxane. Instead, predominant Si−C bond cleavage was observed, even though the reaction was performed under mild conditions. This cleavage leads to the corresponding methylated amine and silica. Owing to the facile elimination of silica by simple filtration, this reaction has been exploited for the synthesis of selective monomethylated primary amines in a one-pot reaction.

Experimental Section

Materials and General Information: All the reactions were performed under nitrogen atmosphere using Schlenk tube techniques. The solvents were distilled under nitrogen over P_2O_5 or Mg turnings before use. Commercially available compounds were purchased from Aldrich, Acros, Gelest or Lancaster and they were used as received without further purification. Optically active (1*R*,2*R*)-diaminocyclohexane was obtained enantiomerically pure from the commercial racemic *cis*/*trans* mixture according to Jacobsen's method.[14] (Chloromethyl)triethoxysilane was prepared by reaction of (chloromethyl)trichlorosilane with ethanol in the presence of triethylamine in an ethereal solution.[15] ^{1}H and ^{13}C NMR spectra in solution were recorded on a Bruker AC-200 spectrometer in

$CDCl_3$. Chemical shifts (δ, ppm) are relative to tetramethylsilane. IR spectra were determined with a Perkin−Elmer 1000 FTIR spectrometer. Mass spectra were measured on a JEOL MS-DX 300 mass spectrometer. Elemental analyses were carried out by the Service Central de Microanalyse du CNRS in Vernaison (France). Optical rotations were measured on a Perkin−Elmer polarimeter 241.

Preparation of 2: Compound **1** was prepared in two steps as already described.[7a,7c] Compound **1** (6 g, 42 mmol), (chloromethyl)triethoxysilane (26.8 g, 126 mmol) and dry triethylamine (12.7 g, 126 mmol) were placed into a glass tube. The tube was then sealed under vacuum and placed in an oven at 130 °C with iron protection. After 18 hours the tube was taken out from the oven and opened at room temperature. The residue was placed in a 100 mL flask, washed with dry pentane and filtered. After evaporation of the solvent, the obtained yellow, viscous liquid was distilled to give **2** as a pale-yellow liquid. Yield: 14 g (68%). $B.p._{0.009}$ = 137 °C. $[\alpha]_D^{20}$ = −15.4 (*c* = 0.4, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ = 1.00−1.12 (m, 4 H, CH_2−CH_2−CH−N), 1.16 (t, 18 H, CH_3−CH_2−O), 1.61−1.72 (m, 4 H, CH_2−CH−N), 2.05−2.34 (m, 2 H, CH−N, 4 H, N−CH_2−Si), 2.17 (s, 3 H, CH_3−NH), 2.26 (s, 6 H, CH_3−N), 3.76 (q, 12 H, CH_2−O) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 18.2 (CH_3−CH_2), 24.2 (CH_2−CH_2−CH−N), 25.8 (CH_2−CH−N), 38.8 (N−CH_2−Si), 39.3 (CH_3−N), 58.2 (CH_2−O), 65.8 (CH−N) ppm. ^{29}Si NMR (200 MHz, $CDCl_3$): δ = −50.1 ppm. MS [FAB (+)]: *m*/*z* (%) = 495 (12) [M +1]. $C_{22}H_{50}N_2O_6Si_2$ (494.32): calcd. C 53.41, H 10.18, N 5.66; found C 53.44, H 10.20, N 5.68.

Preparation of 3 by Hydrolysis of 2: The bis-silylated compound **2** (3 g, 6 mmol) in dry ethanol (6 mL) was placed in a glass tube whilst stirring at room temperature. Distilled water (18 mmol) and NH_4F 1 M (6 μL, 0.1% mol) were then added. A gel formed after 1 min, disappeared after 24 h and a new stable gel formed after 3 days. After 1 week, the gel was crushed and the powder obtained was washed with diethyl ether, filtered and dried under vacuum at 60 °C during 24 h to yield a white powder corresponding to the xerogel (0.97 g).

Identification of 3: The hybrid gel (0.35 g) was introduced into a 10 mL flask and placed under vacuum at 150 °C. The flask was then cooled to −100 °C. After 2 hours of distillation, a yellow liquid (0.07 g) corresponding to **3** was collected at room temperature; the residual solid weighed 0.22 g.

Liquid: ^1H NMR (200 MHz, $CDCl_3$): δ = 1.04−1.23 (m, 4 H, CH_2−CH_2−CH−N), 1.67−1.83 (m, 4 H, CH_2−CH−N), 2.24 (s, 12 H, CH_3−N), 2.28−2.37 (m, 2 H, CH−N) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 22.9 (CH_2−CH_2−CH−N), 25.6 (CH_2−CH−N), 38.8 (N−CH_2−Si), 40.1 (CH_3−N), 63.8 (CH−N) ppm.

Residual Solid: FT-IR (KBr): $\tilde{\nu}$ = 3427, 1096 cm^{-1}. ^{29}Si CP-MAS NMR: δ = −92.6 (Q^2), −102.3 (Q^3), −110 (Q^4) ppm. SiO_2 (59.97): calcd. Si 46.66, O 53.33; found Si 43.00, O 45.75.

Preparation of 10: Compound **1** (6 g, 42 mmol), (chloromethyl)trimethylsilane (15.5 g, 126.7 mmol) and dry triethylamine (12.8 g, 126.7 mmol) were placed in a glass tube. The tube was then sealed under vacuum and placed in a drying oven at 130 °C with an iron protection. After 18 hours the tube was taken out from the oven and opened at room temperature. The residue was placed in a 100 mL flask, washed with dry pentane and filtered. After evaporation of the solvent, the obtained yellow, viscous liquid was distilled. Yield: 10 g (76%). $B.p._{0.009}$ = 105 °C. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.04 (s, 18 H, CH_3−Si), 1.04−1.09 (m, 4 H, CH_2−CH−CH−NH), 1.66−1.78 (m, 4 H, CH_2−CH−N), 2.04 (dd, 4 H, CH_2−Si), 2.26 (s, 6 H, CH_3−N), 2.36−2.37 (m, 2 H, CH−N) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = −1.3 (Si−CH_3), 24.9 (CH_2−CH_2−CH), 25.6 (CH_2−CH−N), 40.2 (N−CH_3), 44.8 (N−CH_2−Si), 66.3 (CH−N) ppm. ^{29}Si NMR (200 MHz, $CDCl_3$): δ = −0.8 ppm. $C_{16}H_{38}N_2Si_2$ (314.26): calcd. C 61.14, H 12.10, N 8.91; found C 61.76, H 12.22, N 9.00.

Preparation of 11: The same protocol as above was used, with **1** (7 g, 50 mmol), (chloromethyl)ethoxydimethylsilane (22.6 g, 150 mmol) and dry triethylamine (15.2 g, 150 mmol). Yield: 14 g (75%). $B.p._{0.02}$ = 120 °C. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.11 (s, 12 H, CH_3−Si), 1.09−1.19 (m, 4 H, CH_2−CH_2−CH−NH), 1.15 (t, 18 H, CH_3−CH_2), 1.64−1.75 (m, 4 H, CH_2−CH−N), 2.05 (dd, 4 H, N−CH_2−Si), 2.22 (s, 6 H, CH_3−N), 2.25−2.31 (m, 2 H, CH−N), 3.60 (q, 12 H, CH_2−O) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = −1.73 (Si−CH_3), 18.5 (CH_3−CH_2), 24.8 (CH_2−CH_2−CH), 25.8 (CH_2−CH−N), 39.9 (N−CH_3), 44.1 (N−CH_2−Si), 58.2 (CH_2−O), 66.5 (CH−N) ppm. $C_{18}H_{42}N_2O_2Si_2$ (374.71): calcd. C 57.75, H 11.22, N 7.48; found C 58.27, H 11.51, N 7.67.

Preparation of 12: The same protocol as above was used, with *N*−methylaminocyclohexane (5 g, 44 mmol), (chloromethyl)triethoxysilane (5.4 g, 44 mmol) and dry triethylamine (4.5 g, 44 mmol). Yield: 12 g (94%). $B.p._{0.025}$ = 80 °C. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.07−1.27 (m, 6 H, CH_2−CH_2−CH−NH), 1.15 (t, 9 H, CH_3−CH_2), 1.54−1.75 (m, 5 H, CH_2−CH−N), 2.01 (s, 2 H, N−CH_2−Si), 2.26 (m, 3 H, CH_3−N), 3.80 (q, 6 H, CH_2−O) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 18.2 (CH_3−CH_2), 26.0 (CH_2−CH_2−CH_2−CH−N), 26.4 (CH_2−CH_2−CH−N), 27.8 (CH_2−CH−N), 37.9 (N−CH_2−Si), 40.9 (CH_3−N), 58.5 (CH_2−O), 64.9 (CH−N) ppm. $C_{14}H_{31}NO_3Si$ (289.21): calcd. C 58.83, H 10.72, N 4.84; found C 59.18, H 10.99, N 4.93.

Preparation of 13: The same protocol as above was used, with piperidine (10 g, 117.6 mmol), (chloromethyl)triethoxysilane (25 g, 117.6 mmol) and dry triethylamine (12 g, 117.6 mmol). Yield: 28.5 g (90%). $B.p._{0.02}$ = 90 °C. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.19 (t, 9 H, CH_3−CH_2), 1.31−1.45 (m, 2 H, CH_2−CH_2−CH−N), 1.48−1.58 (m, 4 H, CH_2−CH_2−N), 1.92 (s, 2 H, N−CH_2−Si), 2.30−2.34 (m, 4 H, CH_2−N), 3.80 (q, 6 H, CH_2−O) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 18.1 (CH_3−CH_2), 23.7 (CH_2−CH_2−CH−N), 26.2 (CH_2−CH_2−N), 44.8 (N−CH_2−Si), 58.1 (CH_2−O), 58.4 (CH_2−N) ppm. ^{29}Si NMR (200 MHz, $CDCl_3$): δ = −50.1 ppm.

General Procedure for the Preparation of 15: The amine **14** (11.67 g, 102 mmol) and (chloromethyl)triethoxysilane (10.87 g, 51 mmol) were placed in a glass tube. The tube was then sealed under vacuum and placed in a drying oven at 87 °C with an iron protection. After 18 hours the tube is taken out from the oven and opened at room temperature. The residue was placed in a 100 mL flask, washed with dry pentane and filtered. After evaporation of the solvent, the obtained yellow, viscous liquid was distilled to give **15**.

15a: Yield: 65%. $B.p._{0.01}$ = 97 °C. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.10−1.20 (m, 4 H, CH_2−CH_2−CH−N), 1.13 (t, 9 H, CH_3−CH_2), 1.57−1.76 (m, 4 H, CH_2−CH_2−NH_2), 1.97−2.17 (m, 4 H, CH_2−CH−N, CH−NH_2), 2.01 (s, 2 H, N−CH_2−Si), 2.57−2.62 (m, 1 H, NH), 3.80 (q, 6 H, CH_2−O) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 18.2 (CH_3−CH_2), 25.2 (CH_2−CH−NH), 25.3 (CH_2−CH_2−CH−NH), 30.3 (CH_2−CH−NH), 30.4 (CH_2−CH−NH), 35.6 (N−CH_2−Si), 54 (CH−NH_2), 58.6 (CH_2−O), 67.2 (CH−NH) ppm. ^{29}Si NMR (200 MHz, $CDCl_3$): δ = −50.2 ppm. $C_{13}H_{30}N_2O_3Si$ (290.20): calcd. C 53.79, H 10.74, N 9.65; found C 55.45, H 10.6, N 9.95.

15c: Yield: 71%. B.p.$_{0.01}$ = 105 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.24 (q, 9 H, CH_3−CH_2), 1.30 (m, 1 H, NH), 2.16 (s, 2 H, N−CH_2−Si), 3.79 (s, 2 H, C_6H_5−CH_2−NH), 3.86 (t, 6 H, CH_2−O), 7.28−7.31 (m, 5 H, C_6H_5) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 18.3 (*C*H_3−CH_2), 33.4 (N−*C*H_2−Si), 57.7 (C_6H_5−CH_2−N), 58.6 (*C*H_2−O), 126 (C_{aryl}-H), 128 (C_{aryl}-H), 140 (C_{aryl}) ppm. ^{29}Si NMR (200 MHz, $CDCl_3$): δ = −50.2 ppm.

15d: Yield: 80%. B.p.$_{0.01}$ = 97 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.29 (t, 9 H, CH_3−CH_2), 2.60 (s, 2 H, N−CH_2−Si), 3.90 (q, 6 H, CH_2−O), 6.60−6.75 (m, 3 H, C_6H_5), 7.16−7.31 (m, 2 H, C_6H_5) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 18.8 (*C*H_3−CH_2), 28.2 (N−*C*H_2−Si), 59.4 (*C*H_2−O), 113 (C_{aryl}-H), 117.6 (C_{aryl}-H), 129.6 (C_{aryl}-H), 150.6 (C_{aryl}) ppm. ^{29}Si NMR (200 MHz, $CDCl_3$): δ = −51.0 ppm. $C_{13}H_{23}NO_3Si$ (269.15): calcd. C 57.90, H 8.60, N 5.19; found C 57.96, H 8.56, N 5.27.

15e: Yield: 67%. B.p.$_{0.01}$ = 115 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.17 (t, 9 H, CH_3−CH_2O), 1.42 (s, 1 H, NH), 2.06 (dd, 2 H, NH−CH_2−Si), 2.89 (s, 2 H, C_6H_5−CH_2−NH), 3.43 (t, 1 H, CH), 3.60 (s, 3 H, CH_3−O), 3.73 (q, 6 H, CH_2−O), 7.13−7.20 (m, 5 H, C_6H_5) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 18.2 (*C*H_3−CH_2), 32.2 (NH−CH_2−Si), 39.3 (C_{aryl}−CH_2), 51.4 (*C*H_3−O), 58.6 (*C*H_2−O), 66.3 (CH), 126.5 (C_{aryl}-H), 128.3 (C_{aryl}-H), 129.2 (C_{aryl}-H), 137.6 (C_{aryl}), 174.8 (*C*O) ppm. ^{29}Si NMR (200 MHz, $CDCl_3$): δ = −51.5 ppm. $C_{17}H_{29}NO_5Si$ (355.18): calcd. C 57.45, H 8.22, N 3.94; found C 56.55, H 7.74, N 4.36.

Preparation of 16 by Hydrolysis of 15: Dry ethanol (10 mL), the silylated amine **15** (9.6, 33 mmol) and distilled water (1.8 g, 99 mmol) were introduced into a 50 mL flask. The reaction medium was then aged at 60 °C for 2 days. The solid formed was separated by filtration, washed with acetone and concentrated under vacuum. The product **16** was obtained as a yellow liquid.

16a: Yield: 98%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.10−1.21 (m, 4 H, CH_2−CH_2−CH−NH_2), 1.66−1.99 (m, 4 H, CH_2−CH), 2.19−2.30 (m, 2 H, N−C*H*−CH), 2.32 (s, 3 H, CH_3N) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 25.0 (*C*H_2−CH_2−CH−NH_2), 25.2 (CH_2−CH_2−CH−NH), 30.4 (*C*H_2−CH−NH_2), 33.5 (*C*H_2−CH−NH−CH_3), 36.1 (*C*H_3−NH), 54.9 (*CH*−NH_2), 65.4 (*C*H−NH−CH_3) ppm.

16c: Yield: 84%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.23 (s, 3 H, NH−CH_3), 3.41 (s, 2 H, C_6H_5−CH_2), 7.20−7.32 (m, 5 H, C_6H_5) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 43.4 (*C*H_3−NH), 57.7 (C_6H_5−CH_2−N), 126.7 (C_{aryl}-H), 128.1 (C_{aryl}-H), 140.3 (C_{aryl}) ppm.

16d: Yield: 63%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.93 (s, 3 H, N−CH_3), 7.14−7.19 (m, 3 H, C_6H_5), 7.25−7.36 (m, 2 H, C_6H_5) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 37.8 (*C*H_3−NH), 121.0 (C_{aryl}-H), 128.1 (C_{aryl}-H), 129.5 (C_{aryl}-H), 138.6 (C_{aryl}) ppm.

16e: Yield: 70%. ^{1}H NMR (200 MHz, $CDCl_3$): ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.34 (s, 3 H, CH_3−N), 2.93 (d, 2 H, C_6H_5−CH_2), 3.43 (t, 1 H, C*H*−N), 3.63 (s, 3 H, CH_3−O), 7.17−7.25 (m, 5 H, C$_6H_5$) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 34.7 (C_6H_5−CH_2−N), 39.5 (*C*H_3−N), 51.6 (*C*H_3−O), 64.6 (*C*H−N), 126.7 (C_{aryl}-H), 128.5 (C_{aryl}-H), 129.1 (C_{aryl}-H), 137.1 (C_{aryl}), 174.7 (*C*O) ppm. MS [FAB (+)] *m*/*z* (%) = 194 (100) [M + 1]. $C_{11}H_{15}NO_2$ (193.11): calcd. C 68.37, H 7.82, N 7.25; found C 69.02, H 7.93, N 7.47.

Preparation of 16b, 16d and 16e in One Step: The amine (33.5 mmol) and (chloromethyl)trimethylsilane (3.56 g, 16.75 mmol) were introduced into a glass tube. The tube was then sealed under vacuum and placed in a drying oven at 87 °C with an iron protection. After 18 hours the tube was taken out from the oven and opened at room temperature. The residue was placed in a 100 mL flask, washed with dry pentane and filtered. After evaporation of the solvent, the obtained yellow, viscous liquid was refluxed in a mixture of water (2.9 mL) and ethanol (10 mL) for 2 days. The residue was then filtered and concentrated to give the pure methylated amine.

16b: Yield: 68%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.05−1.25 (m, 6 H, CH_2−CH_2−CH_2−CH−N), 1.58−1.82 (m, 4 H, CH_2−CN−CH_2), 2.25−2.35 (m, 1 H, N−CH), 2.39 (s, 3 H, CH_3N) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 24.6 (CH_2), 25.8 (CH_2−CH_2−CH_2), 32.8 (*C*H_2−CH−N), 33.2 (*C*H_3−NH), 54.9 (*CH*−N) ppm.

16d: Yield: 80%.

16e: Yield: 88%.

[1] [1a] C. J. Brinker, G. W Scherer, *Sol-Gel Science: the Physics and Chemistry of Sol-Gel Processing*, Academic Press, San Diego, **1990**. [1b]C. Sanchez, F. Ribot, *New J. Chem.* **1994**, *18*, 1007−1047. [1c] *Organic/Inorganic Hybrid Materials. MRS Symp. vol. 519* (Eds. R. M. Laine, C. Sanchez, C. J. Brinker, E. Giannelis), **1998**. [1d] *Organic/Inorganic Hybrid Materials. MRS Symp. vol. 628* (Eds. R. M. Laine, C. Sanchez, C. J. Brinker), **2000**.

[2] [2a] K. J. Shea, D. A. Loy, O. W. Webster, *Chem. Mater.* **1989**, *1*, 512−513. [2b] K. J. Shea, D. A. Loy, O. W. Webster, *J. Am. Chem. Soc.* **1992**, *114*, 6700−6710. [2c] D. A. Loy, K. J. Shea, *Chem. Rev.* **1995**, *95*, 1431−1442.

[3] [3a] R. J. P. Corriu, J. J. E. Moreau, P. Thépot, M. Wong Chi Man, *Chem. Mater.* **1992**, *4*, 1217−1224. [3b] R. J. P. Corriu, D. Leclercq, *Angew. Chem.* **1996**, *108*, 1524−1540; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1420−1436.

[4] [4a] U. Schubert, *New J. Chem.* **1994**, *18*, 1049−1058. [4b] H. W. Oviatt, K. Shea, S. Kalluri, Y. Shi, W. H. Steier, L. R. Dalton, *Chem. Mater.* **1995**, *7*, 493−498. [4c] B. Lebeau, S. Brasselet, J. Zyss, C. Sanchez, *Chem. Mater.* **1997**, *9*, 1012−1021. [4d] S. Bourg, J-C. Broudic, O. Conocar, J. J. E. Moreau, D. Meyer, M. Wong Chi Man, *Chem. Mater.* **2001**, *13*, 491−499. [4e] C. Sanchez, G. J. de A. A. Soler-Illia, F. Ribot, T. Lalot, C. R. Mayer, V. Cabuil, *Chem. Mater.* **2001**, *13*, 3061−3083. [4f] G. J. de A. A. Soler-Illia, C. Sanchez, B. Lebeau, J. Patarin, *Chem. Rev.* **2002**, *102*, 4093−4138. [4g] C. Sanchez, G. J. de A. A. Soler-Illia, F. Ribot, D. Grosso, *C. R. Chim.* **2003**, *6*, 1131−1151.

[5] [5a] J. J. E. Moreau, L. Vellutini, M. Wong Chi Man, C. Bied, *J. Am. Chem. Soc.* **2001**, *123*, 1509−1510. [5b] C. Bied, J. J. E. Moreau, L. Vellutini, M. Wong Chi Man, *J. Sol-Gel. Sci. Technol.* **2003**, *26*, 583−586.

[6] [6a] J. J. E Moreau, L. Vellutini, M. Wong Chi Man, C. Bied, J.-L. Bantignies, P. Dieudonné, J.-L. Sauvajol, *J. Am. Chem. Soc.* **2001**, *123*, 7957−7958. [6b] J. J. E. Moreau, L. Vellutini, M. Wong Chi Man, C. Bied, J.-L. Bantignies, P. Dieudonné, J.-L. Sauvajol, *Mater. Res. Soc. Symp. Proc.* **2002**, *726*, 235−242. [6c] J. J. E Moreau, L. Vellutini, M. Wong Chi Man, C. Bied, *Chem. Eur. J.* **2003**, *9*, 1594−1599. [6d] J. J. E Moreau, B. P. Pichon, M. Wong Chi Man, C. Bied, H. Pritzkow, J.-L. Bantignies, P. Dieudonné, J.-L. Sauvajol, *Angew. Chem.* **2004**, *116*, 205−208; *Angew. Chem. Int. Ed.* **2004**, *43*, 203−206.

[7] [7a] A. Adima, J. J. E. Moreau, M. Wong Chi Man, *J. Mater. Chem.* **1997**, *7*, 2331−2333. [7b] J. J. E. Moreau, M. Wong Chi Man, *Coord. Chem. Rev.* **1998**, *178−180*, 1073−1084. [7c] A. Adima, J. J. E. Moreau, M. Wong Chi Man, *Chirality* **2000**, *12*, 411−420. [7d] C. Bied, D. Gauthier, J. J. E Moreau, M. Wong Chi Man, *J. Sol-Gel Sci. Technol.* **2001**, *20*, 313−320. [7e] A. Brethon, J. J. E. Moreau, M. Wong Chi Man, *Tetrahedron: Asymmetry* **2004**, *15*, 495−502.

[8] M. Fiorini, G. M. Giongo, *J. Mol. Catal.* **1979**, *5*, 303−308.

[9] [9a] C. Eaborn, N. Retta, J. D. Smith, *J. Chem. Soc., Dalton Trans.* **1983**, 905−909. [9b] R. Brost, G. C. Bruce, S. L. Grundy, S. R. Stobart, *Inorg. Chem.* **1993**, *32*, 5195−5200.

[10] [10a] Y. Sato, H. Sakakibara, *J. Organomet. Chem.* **1979**, *166*, 303−307. [10b] Y. Sato, Y. Yargi, M. Koto, *J. Org. Chem.* **1980**, *45*, 613−617. [10c] M. Hori, Y. Sato, N. Shirai, F. Sumiya, *J. Org. Chem.* **1989**, *54*, 836−840.

[11] [11a] R. Tacke, J. Becht, O. Dannapel, R. Ahlrichs, U. Schneider, W. S. Sheldrick, J. Hahn, F. Kiesgen, *Organometallics* **1996**, *15*, 2060−2077. [11b] R. Tacke, B. Ulmer, B. Wagner, M. Arlt, *Organometallics* **2000**, *19*, 5297−5309. [11c] A. R. Bassindale, Y. I. Baukov, P. G. Taylor, V. V. Negrebetsky, *J. Organomet. Chem.* **2002**, *655*, 1−6.

[12] [12a] S. Krishnamurthy, *Tetrahedron. Lett.* **1982**, *23*, 3315−3318. [12b] R. Grigg, T. R. B. Mitchell, *J. Chem. Soc., Chem. Commun.* **1981**, 611−612. [12c] S. B. Kadin, *J. Org. Chem.* **1973**, *38*, 1348−1350. [12d] M. Selva, A. Bomben, P. Tundo, *J. Chem. Soc., Perkin Trans. 1* **1997**, *1*, 1041−1045. [12e] E. M. Briggs, G. W. Brown, J. Jiricny, M. F. Meidine, *Synth. Commun.* **1980**, 295−296. [12f] M. D. M. Gray, D. J. H. Smith, *Tetrahedron Lett.* **1980**, *21*, 859−860. [12g] J. Zwierzak, J. Brylikowska-Piotriwicz, *Angew. Chem.* **1977**, *89*, 552−553; *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 107−108. [12h] T. Takata, A. Maturu, *Tetrahedron Lett.* **1984**, *34*, 3631−3632. [12i] S. Padmanabhan, N. L. Reddy, G. J. Durant, *Synth. Commun.* **1997**, *27*, 691−699.

[13] [13a] N. Shirai, Y. Sato, *J. Org. Chem.* **1988**, *53*, 194−196. [13b] T. Tanaka, N. Shirai, Y. Sato, *Chem. Pharm. Bull.* **1992**, *40*, 518−520.

[14] J. F. Larrow, E. N. Jacobsen, *J. Org. Chem.* **1994**, *59*, 1939−1942.

[15] [15a] J. E. Noll, J. L. Speier, B. F. Daubert, *J. Am. Chem. Soc.* **1951**, *73*, 3867−3871. [15b] J. L. Speier, C. A. Roth, J. W. Ryan, *J. Org. Chem.* **1971**, *36*, 120−126. [15c] D. Brondani, R. J. P. Corriu, S. El Ayoubi, J. J. E. Moreau, M. Wong Chi Man, *Tetrahedron Lett.* **1993**, *34*, 2111−2114.

Received February 6, 2004

