# Amine and ester-substituted silsesquioxanes: synthesis, characterization and use as a core for starburst dendrimers

Frank J. Feher* and Kevin D. Wyndham

Department of Chemistry, University of California, Irvine, CA 92697-2025, USA

Practical procedures are reported for the syntheses of amine and ester-substituted silsesquioxane frameworks with the formula $R_8Si_8O_{12}$ with R = $CH_2CH_2CH_2NH_2$ (2), $[CH_2CH_2CH_2NH_3]Cl$ (3) and $CH_2CH_2CMe_2CH_2CO_2Me$ (4); the use of 2 as a core for starburst dendrimers with R = $CH_2CH_2CH_2N(CH_2CH_2CO_2Me)_2$ (5) and $CH_2CH_2CH_2N(CH_2CH_2C(O)NHCH_2CH_2NH_2)_2$ (6) is also described.

Polyhedral oligosilsesquioxanes (POSS) are an interesting class of clusters derived from the hydrolytic condensation of trifunctional organosilicon monomers.[1–3] Cube-octameric clusters (*e.g.* **1**) are most common, but a wide variety of other polyhedral frameworks have been identified. Interest in POSS has grown rapidly over the past several years, particularly for polymer-related applications, where several families of POSS monomers have been developed as precursors to hybrid inorganic–organic polymers.[4] Many other applications for POSS have emerged and developed rapidly as straightforward procedures have been devised for preparing frameworks with synthetically useful pendant groups.[5–9] Here, we report practical syntheses of several new silsesquioxanes that are attractive starting materials for more elaborate molecules, including amine- and ester-substituted frameworks that have excellent potential as cores for starburst dendrimers.


1	R = alkyl, vinyl or aryl
2	$CH_2CH_2CH_2NH_2$
3	$[CH_2CH_2CH_2NH_3]Cl$
4	$CH_2CH_2CMe_2CH_2CO_2Me$
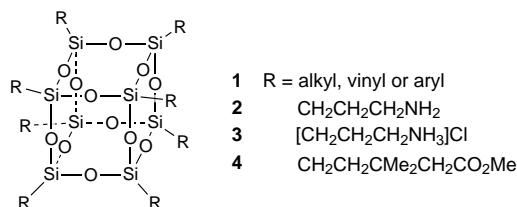
Wacker-Chemie's 1991 US patent[10] claimed the preparation of **2**. This compound is ideally suited for many purposes, but no experimental details or characterization data were provided in the patent. We reinvestigated these claims and now confirm that the hydrolytic condensation of γ-aminopropyltriethoxysilane in MeOH–conc. HCl does indeed provide easy access to an amine-substituted framework,† but the product obtained under conditions reported by Wacker-Chemie is **3** rather than **2** (*i.e.* the free amine).[11] This hydrochloride is highly soluble in water (> 0.9 g ml^{-1}), poorly soluble or insoluble in most organic solvents and is somewhat hygroscopic. It is also surprisingly difficult to neutralize without destroying the Si/O framework, but neutralization of **3** to **2** can be accomplished by eluting solutions of **3** in methanol or 14 : 1 ethanol–water solutions across a column of Amberlite IRA-400 resin.‡ The resulting solution of **2** appears to be stable for 1–2 days at 25 °C, but decomposes to an ill-defined T-gel upon prolonged storage at 25 °C or when the solvent is removed.

It is interesting to note that a ^{29}Si NMR spectrum of the decomposition product is nearly identical to the published spectrum for products from the uncatalyzed hydrolysis γ-aminopropyltriethoxysilane in 14 : 1 EtOH–H$_2$O.[12] Both

spectra exhibit several sharp resonances between δ −60 and −72, including a large resonance at δ −68.5 previously assigned[12] to **2**, but the characteristic resonance for pure **2** only appears as a minor resonance at δ −66.8. In light of the fact that MALDI-TOF mass spectra of both samples exhibit many peaks at m/z < 3000, but no large peaks attributable to $R_nSi_nO_{3n/2}$ (n = 6, 8, 10, 12), it appears that fully condensed frameworks containing free aminopropyl groups are not stable relative to incompletely condensed frameworks and/or T-gels.

Platinum-catalyzed hydrosilylation reactions of $H_8Si_8O_{12}$ provide convenient access to a wide variety of functionalized silsesquioxanes,[5,6,9,13,14] but in most cases the products are complicated mixtures of isomers because both α- and β-addition to the alkene are observed. Gentle and Bassindale[5] noted that β-addition and a number of side-reactions can be suppressed by increasing steric bulk on the γ-position and avoiding the use of vinyl silanes as alkenes. We have found that β-addition can be completely eliminated by using 3,3-disubstituted α-alkenes. In the case of $H_8Si_8O_{12}$[15] and readily available $H_2C=CHCMe_2CH_2CO_2Me$ (Aldrich), hydrosilylation with Speier's catalyst is complete within 48 h in refluxing hexanes to produce high yields of **4**, which spontaneously crystallizes from solution as large colorless crystals.§ We have not examined other hydridosilsesquioxanes (*e.g.* $H_{10}Si_{10}O_{15}$, $H_{12}Si_{12}O_{18}$, $H_{14}Si_{14}O_{21}$),[15,16] but these compounds should react similarly with $H_2C=CHCMe_2CH_2CO_2Me$ to produce isomerically pure derivatives containing ester-substituted pendant groups on each vertex. Ester-substituted frameworks should also be available from analogous Pt-catalyzed reactions of $H_2C=CHCMe_2CH_2CO_2Me$ with readily available hydride-substituted spherosilicates [*e.g.* $(HSiMe_2O)_8Si_8O_{12}$].[10]

5	X = OMe
6	$NHCH_2CH_2NH_2$
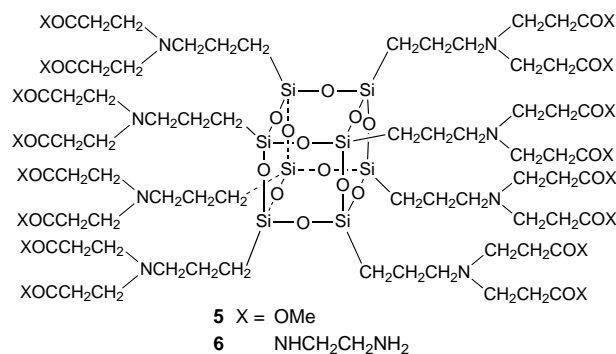
An interesting ester-substituted framework can also be prepared *via* the reaction of **2** with methyl acrylate. When performed under conditions typically used to prepare PAMAM dendrimers from polyamine cores,[17,18] this reaction produces excellent yields of **5**; subsequent reaction of **5** with an excess of ethylenediamine produces **6**. Both **5** and **6** were identified on the basis of multinuclear NMR data and MALDI-TOF mass spectra.¶ Higher generation PAMAM dendrimers with a Si_8O_{12} core can presumably be synthesized by further synthetic iterations.

In summary, we have developed straightforward procedures for the synthesis of amine and ester-substituted silsesquioxane frameworks. We have also demonstrated that silsesquioxanes can be used as cores for the preparation of amine or ester-terminated starburst dendrimers. The use of silsesquioxanes as cores for dendrimers is particularly attractive[6] because their polyhedral structures should produce spherically symmetric dendrimers with smaller generation numbers then more conventional cores.[19] Our efforts to use amine and ester-substituted silsesquioxanes as building blocks for hybrid inorganic–organic materials[4,20] and as platforms for biologically active pendant groups will be reported separately.

Notes and References

* E-mail: fjfeher@uci.edu

† The reaction of $H_2NCH_2CH_2CH_2Si(OEt)_3$ (150 ml, 0.627 mol) and conc. HCl (200 ml) in MeOH (3.6 l) produces **3** (30%) as a microcrystalline solid after 6 weeks at 25 °C. The crude product obtained after filtration, washing with MeOH and drying (0.001 Torr, 25 °C) is spectroscopically pure. Recrystallization from MeOH affords **3** as white microcrystalline powder. ^1H NMR [500.2 MHz, $(CD_3)_2SO$, room temp.] δ 8.25 (s, NH_3, 24 H), 2.75 (t, CH_2NH_3, 16 H), 1.71 (m, $SiCH_2CH_2$, 16 H), 0.71 (t, $SiCH_2$, 16 H). $^{13}C\{^1H\}$ NMR [125.8 MHz, $(CD_3)_2SO$, room temp.] δ 41.01 (s, CH_2NH_3), 20.61 (s, $SiCH_2CH_2$), 8.44 (s, $SiCH_2$). ^{29}Si NMR [99.4 MHz, $(CD_3)_2SO$, room temp.] δ −66.4 (s). IR (KBr): 3190, 3023, 2903, 1579, 1506, 1215, 1138, 1110, 994, 923, 808, 706 cm^{-1}. Anal. for $C_{24}H_{72}O_{12}Si_8N_8C_{18}$ (calc.): 24.69 (24.57), 6.40 (6.19), 9.40 (9.55%). Mass spectrum (MALDI-TOF, DHB matrix), m/z (relative intensity), 881.4 ($[M + H − 8 HCl]^+$, 100%), 863.4 ($[M − NH_3]^+$, 39%).

‡ Amberlite IRA-400 ion-exchange resin (37 g) is prepared by successive washing with H_2O (4 × 200 ml), 1 M NaOH (3 × 200 ml), H_2O (6 × 200 ml) and finally MeOH or 14 : 1 EtOH–H_2O (6 × 200 ml). Half of the beads are loaded onto a column (3.5 cm o.d.); the other half are used to dissolve a suspension of **3** (5 g) in a minimum amount of MeOH or EtOH–H_2O. Elution across the column produces a stock solution of **2** which tests negative for chloride. Small samples of **2** can be prepared by rapidly evaporating aliquots from the stock solution, but to avoid decomposition, the amine should be prepared immediately before use or stored in MeOH solutions at −35 °C. ^1H NMR (500.2 MHz, CD_3OD, room temp.) δ 4.4 (s, NH_2 and H_2O), 2.52 (t, CH_2N, 16 H), 1.46 (m, $SiCH_2CH_2$, 16 H), 0.56 (t, $SiCH_2$, 16 H). $^{13}C\{^1H\}$ NMR (125.8 MHz, CD_3OD, room temp.) δ 44.85 (s, CH_2N), 26.88 (s, $SiCH_2CH_2$), 9.57 (s, $SiCH_2$). ^{29}Si NMR (99.4 MHz, CD_3OD, room temp.) δ −66.4 (s). Mass spectrum (MALDI-TOF, DHB matrix), m/z (relative intensity), 881.5 ($[M + H]^+$, 100%), 863.5 ($[M − NH_3]^+$, 49%).

§ Methyl-3,3-dimethylpent-4-enoate (Aldrich) (11 ml, 0.068 mol) and $[HSiO_{3/2}]_8$ (3.30 g, 7.74 mmol) are reacted (48 h) in refluxing hexanes (8 ml) with a catalytic amount of Speier's catalyst as described in ref. 5; the yield is quantitative by ^1H, ^{13}C and ^{29}Si NMR spectroscopy. Upon cooling, ester **4** crystallizes as large colorless crystals (80%). ^1H NMR (500.1 MHz, $CDCl_3$, room temp.) δ 3.62 (s, OCH_3, 24 H), 2.179 (s, CH_2CO, 16 H), 1.401 (m, $SiCH_2CH_2$, 16 H), 0.959 (s, CH_3, 48 H), 0.567 (m, 16 H, $SiCH_2$). $^{13}C\{^1H\}$ NMR (127.8 MHz, $CDCl_3$, room temp.) δ 172.70 (s, CO), 51.02, 44.95, 35.31, 33.80 (s, $SiCH_2CH_2$), 26.48 (s, CH_3), 6.06 (s, $SiCH_2$). Anal. for $C_{64}H_{120}O_{28}Si_8$ (calc.): 49.59 (49.20), 7.72 (7.74%). Mass spectrum (EI,

70 eV, 200 °C), m/z (relative intensity), 1529.5 ($[M − OCH_3]^+$ 100%), 1417.3 ($[M − C_8H_{15}O_2]^+$, 40%).

¶ Ester **5** was prepared in 73% yield (204 mg) *via* the reaction (room temp., 24 h) of methyl acrylate (0.8 ml, 8.884 mmol) with freshly prepared **2** (65 mg, 0.029 mmol) in methanol (1 ml).[18] Subsesquent reaction of **5** (48 mg 0.021 mmol) with an excess of $H_2NCH_2CH_2NH_2$ (220 equiv. ester, 4 °C, 4 d) afforded **6** in 100% yield (58 mg).[17] For **5**: ^1H NMR (500.2 MHz, CD_3OD, room temp.) δ 3.61 (s, CH_3, 48 H), 2.71 (t, CH_2CO, 32 H), 2.40 [m, $CH_2N(CH_2)$, 48 H] 1.51 (m, $SiCH_2CH_2$, 16 H), 0.593 (t, $SiCH_2$, 16 H). $^{13}C\{^1H\}$ NMR (125.8 MHz, CD_3OD, room temp.) δ 174.53 (s, CO), 57.23 [s, $CH_2N(CH_2)_2$], 52.13 (s, CH_2CO_2), 50.34 (s, CH_3), 33.27 [s, $CH_2N(CH_2)_2$], 21.48 (s, $SiCH_2CH_2$), 10.21 (s, $SiCH_2$). ^{29}Si NMR (99.4 MHz, CD_3OD, room temp.) δ −6.0(s). Mass spectrum (MALDI-TOF, DHB matrix), m/z (relative intensity); 2256.5 ($[M]^+$, 100%). For **6**: ^1H NMR (500.2 MHz, CD_3OD, room temp.) δ 3.18 (t, CH_2, 32 H), 2.70 (t, CH_2, 32 H), 2.66 (t, CH_2, 32 H), 2.43 (t, $SiCH_2CH_2$, 16 H), 2.31 (t, CH_2, 32 H), 1.50 (m, $SiCH_2CH_2$, 16 H), 0.58 (t, $SiCH_2$, 16 H). $^{13}C\{^1H\}$ NMR (125.8 MHz, CD_3OD, room temp.) δ 175.08 (s, CO), 57.13 [s, $CH_2N(CH_2)_2$], 50.81 (s, CH_2), 43.07 (s, CH_2), 42.11 (s, CH_2), 34.57 [s, $CH_2N(CH_2)_2$], 21.12 (s, $SiCH_2CH_2$), 10.57 (s, $SiCH_2$). ^{29}Si NMR (99.4 MHz, CD_3OD, room temp.) δ −66.2 (s). Mass spectrum (MALDI-TOF, DHB matrix), m/z (relative intensity); 2705.5 $[M]^+$.

1 M. G. Voronkov and V. Lavrent'ev, *Top. Curr. Chem.*, 1982, **102**, 199.

2 R. H. Baney, M. Itoh, A. Sakakibara and T. Suzuki, *Chem. Rev.*, 1995, **95**, 1409.

3 H. Bürgy, G. Calzaferri, D. Herren and A. Zhdanov, *Chimia*, 1991, **45**, 3.

4 J. D. Lichtenhan, *Comments Inorg. Chem.*, 1995, **17**, 115.

5 T. E. Gentle and A. R. Bassindale, *J. Inorg. Organomet. Pol.*, 1995, **5**, 281.

6 A. R. Bassindale and T. E. Gentle, *J. Mater. Chem.*, 1993, **3**, 1319.

7 F. J. Feher, D. Soulivong, A. G. Eklund and K. D. Wyndham, *Chem. Commun.*, 1997, 1185.

8 C. Zhang and R. M. Laine, *J. Organomet. Chem.*, 1996, **521**, 199.

9 U. Dittmar, B. J. Hendan, U. Flörke and H. C. Marsmann, *J. Organomet. Chem.*, 1995, **489**, 185.

10 R. Weidner, N. Zeller, B. Deubzer and V. Frey, *US Pat.*, 5,047,492, 1991.

11 (*a*) Similar results have been independently obtained by Gravel and Laine:[11b] (*b*) M.-C. Gravel and R. M. Laine, *ACS Polym. Prepr.*, 1997, **38**, 155.

12 P. M.-T. Olivera-Pastor, E. Rodriguez-Castellon, A. Jimenez-Lopez, T. Cassagneau, D. J. Jones and J. Roziere, *Chem. Mater.*, 1996, **8**, 1758.

13 J. V. Crivello and R. Malik, *J. Polym. Sci., Part A: Polym. Chem.*, 1997, **35**, 407.

14 A. Tsuchida, C. Bolln, F. G. Sernetz, H. Frey and R. Malhaupt, *Macromolecules*, 1997, **30**, 2818.

15 P. A. Agaskar, *Inorg. Chem.*, 1991, **30**, 2707.

16 P. A. Agaskar and W. G. Klemperer, *Inorg. Chim. Acta*, 1995, **229**, 355.

17 D. A. Tomalia, H. Baker, J. R. Dewald, M. Hall, G. Kallos, S. Martin, J. Roeck, J. Ryder and P. Smith, *Polym. J.*, 1985, **17**, 117.

18 A. D. Meltzer, D. A. Tirrell, A. A. Jones, P. T. Inglefield, D. M. Hedstrand and D. A. Tomalia, *Macromolecules*, 1992, **25**, 4541.

19 G. R. Newkome, C. N. Moorefield and F. Vogtle, in *Dendritic Molecules*, New York, 1996.

20 J. D. Lichtenhan, in *Silsesquioxane-Based Polymers*, ed. J. C. Salamone, New York, 1996.