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Synthesis of benzyl-terminated dendrons for use in high-resolution capillary gas chromatography

George R. Newkome,[a,*] Kyung Soo Yoo,[a] Abuzar Kabir[b] and Abdul Malik[b]

[a]*Institute for Polymer Science and Department of Chemistry, The University of Akron, Akron, OH 44325, USA*
[b]*Department of Chemistry, University of South Florida, Tampa, FL 33620, USA*

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Abstract—The synthesis, silane functionalization, and facile silica attachment of dendritic monomers containing terminal benzyl groups are presented. For the first time, a simple one-step procedure is described that leads to the in situ creation of a surface-bonded sol-gel dendritic stationary phase on the inner walls of a fused silica capillary; such phases showed unique selectivities in high-resolution capillary gas chromatography. © 2001 Elsevier Science Ltd. All rights reserved.

In the past decade, highly functionalized branched materials have found use in numerous applications[1] such as host–guest chemistry,[2–5] carbohydrate chemistry,[6–11] metallodendrimers,[12–20] catalysis,[21–26] and surface chemistry.[27] These various applications were made possible due to either internal or external modifications of dendrimers, which possess a general spherical shape, and thus are capable of intermolecular interactions with the immediate environment as well as an inner regime capable of utilitarian supramolecular characteristics.[1] We are not aware of any application of functionalized dendrons as a stationary phase in capillary gas chromatography, although their applications as mobile phase additives in liquid-phase separations have been reported.[28–31] Herein, we describe the synthesis, extended silane functionalization, and a silica attachment procedure for highly branched building blocks containing benzyl ether terminal groups.

Access to the desire dendrons **3**, **8**, and **13** (Fig. 1) was facilitated by the use of the previously reported[32–37] amine and isocyanate monomers **1** and **2**, respectively. Thus, the preparation (Scheme 1) of the nitrobenzyl ether **5** and its larger analog **10** was effected by reaction of 4-amino-4-[3-(benzyloxy)propyl]-1,7-di(benzyloxy)-heptane[32] (**1**) with the triacid[38] **4** and nonacid[39] **9**, respectively, using standard DCC coupling conditions.[40] Formation of the nitrobenzyl ethers **5** and **10** was confirmed (^{13}C NMR) by the observation of an upfield shift of the carbonyl carbon resonance [δ: 173.5 (**4**) and 174.9 (**9**) to 169.9 (**5**) and 171.9 (**10**) ppm] indicating the acid to amide conversion, and a downfield shift [δ: 52.9 (**1**) to 58.1 (**5**) and 57.8 (**10**) ppm] of the signal assigned to the $C^{4°}$moiety in triether **1**. Both structures were further supported by the peaks at m/z 1673.1 [M+Na$^+$] (**5**: calcd m/z 1673.2 [M+Na$^+$]) and m/z 5106.6 [M+Na$^+$] (**10**: calcd m/z 5106.8 [M+Na$^+$]) in ESI-MS and MALDI-TOF, respectively.

Reduction of the nitro groups with NiB and NaBH$_4$[32] in a MeOH–EtOH–C$_6$H$_5$Me mixture at 50°C afforded the corresponding amines **6** and **11**, whose structures were identified by the traditional chemical shift (^{13}C NMR) of the signal for the $C^{4°}$ from 92.4 (**5**) and 93.1 (**10**) ppm to 52.6 (**6**) and 49.3 (**11**) ppm, respectively, thereby confirming the desired $C^{4°}$-NO$_2$ to $C^{4°}$-NH$_2$ transformation.

Treatment of amines **6** and **11** with 0.4 equiv. of triphosgene in the presence of Et$_3$N in CH$_2$Cl$_2$ gave the corresponding isocyanates **7** and **12**. Their structures were characterized (^{13}C NMR) by the absorption of chemical shifts from 52.6 and 49.3 ppm to 61.9 and 60.3 ppm, respectively, corresponding to the $C^{4°}$-NH$_2$ to $C^{4°}$-NCO conversion, as well as the appearance of a new peak at ca. 122 ppm for the N*C*O group. Furthermore, the IR spectrum for each showed the typical isocyanate peak at 2257 and 2248 cm^{-1} and the ESI-MS and MALDI-TOF further confirmed their assignment by a peak at m/z 1646.2 [M$^+$] (**7**: calcd m/z 1646.2 [M$^+$]) and m/z 5080.2 (**12**: calcd m/z 5080.8 [M+H$^+$]), respectively.

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[*] Corresponding author. Tel.: +330-972-6458; fax: +330-972-2413; e-mail: newkome@uakron.edu

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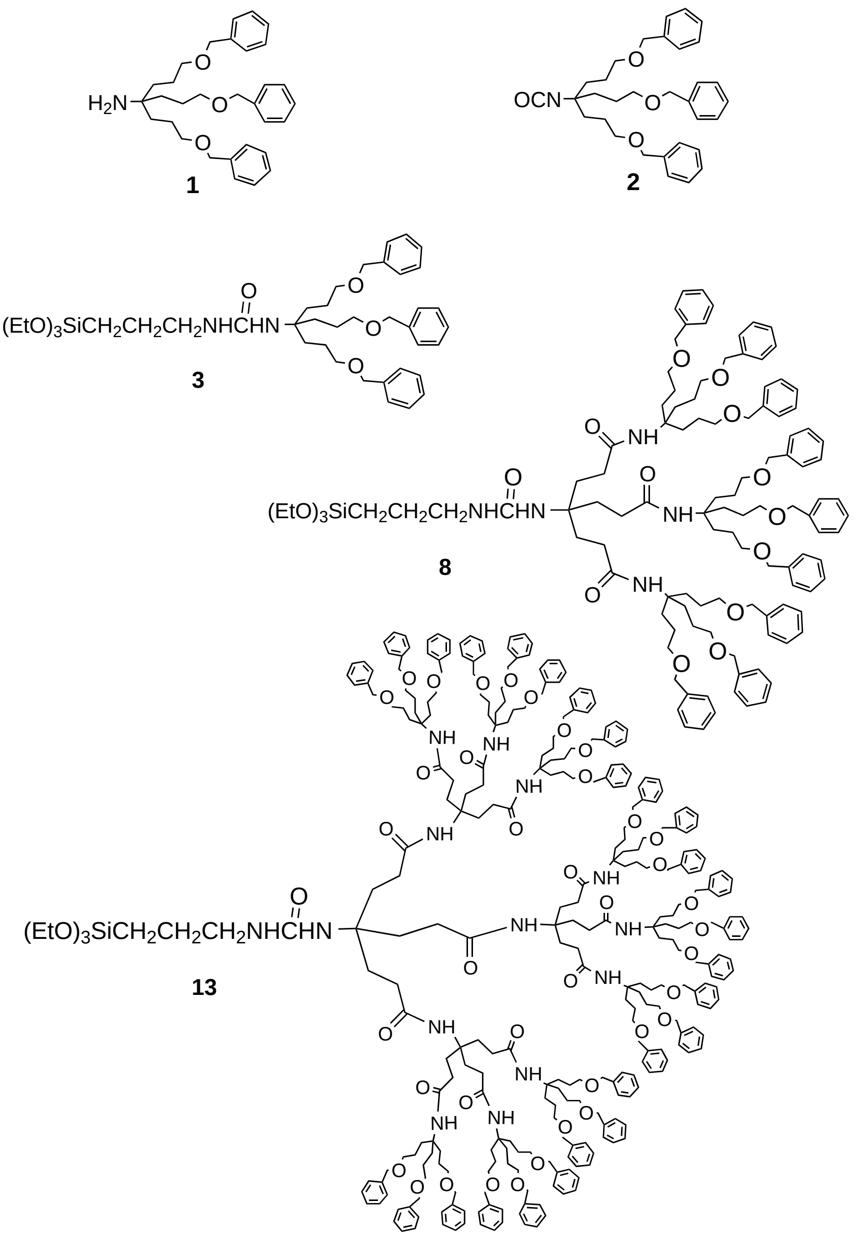
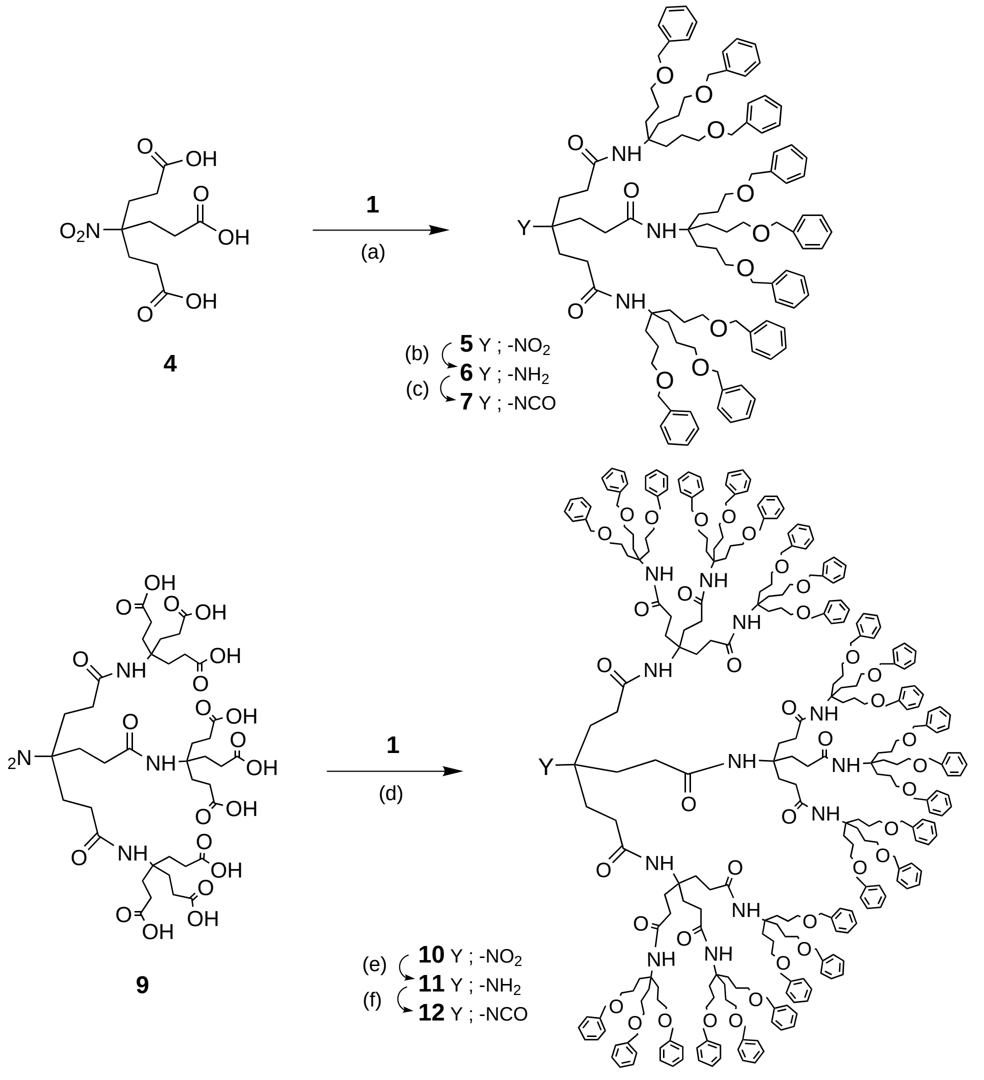


Figure 1.

Dendritic silane reagents **3**, **8**, and **13** were then synthesized by treatment of these monomers possessing the focal isocyanate moiety and terminal benzyloxy groups with 3-(triethoxysilyl)propylamine in dry CH_2Cl_2 at 25°C for 1 h. Their preparation was confirmed (^{13}C NMR) in all cases by the presence of a new urea (NH*C*ONH) carbon peak at ca. 157 ppm, as well as (IR) new absorbance peaks at 1100 and 1650 cm^{-1} for the silane group (Si-O) and urea carbonyl group; the absorbance peak (2250 cm^{-1}) indicative of the -NCO moiety was absent.

Silica attachment of the sol-gel active dendritic reagents (**3**, **8**, or **13**) in the presence of added methyltrimethoxysilane (MTMS), and catalyzed by TFA proceeded smoothly via hydrolysis and subsequent polycondensation to form an organic–inorganic hybrid polymer network with the dendron as the organic constituent. Conducting the reaction within a clean fused silica capillary column provided a simple means for effective column deactivation as well as stationary film immobilization.[41]

Fig. 2 presents three gas chromatograms obtained on three different sol-gel columns with the first (**3**) (A), second (**8**) (B), and third generation (**13**) (C) benzyl-terminated dendritic appendages were incorporated into stationary phases. A Grob test mixture,[42] containing compounds from different chemical classes, was used as the sample probe. As can be seen in Fig. 2, the sol-gel dendrimer stationary phase can provide well-behaved chromatographic peaks for both polar and non-polar components. The elution pattern for individual components of this mixture is very different from that



Scheme 1. Synthesis of second and third generation building blocks: (a, d) DCC, 1-HOBT, 25°C, dry DMF, 48 h; (b, e) $NaBH_4$, NiB, 50°C, MeOH, 1 h; (c) Et_3N, triphosgene, 25°C, CH_2Cl_2, 1.5 h; (f) Et_3N, triphosgene, 55°C, CH_2Cl_2, 1.5 h.

obtained on conventional columns. For example, unlike conventional PDMS or related capillary GC columns that elute 2,3-butanediol as the first peak under standard operating conditions, on benzyl-terminated sol-gel dendrimerized columns, the first eluted component is *n*-decane. In this respect, the sol-gel dendrimerized column behaved more like a polar column (e.g. PEG type) characterized by early elution of *n*-alkanes. A closer look at the chromatograms in Fig. 2 reveals that compared with conventional PDMS column, the functionalized sol-gel column provided a different elution order for all peaks (except for methyl dodecanoate, which elutes last in both cases). This selectivity of the sol-gel functionalized stationary phase in GC may be attributed to the specific molecular architecture of these modified stationary phases. A marked difference in chromatographic selectivity is observed between different generations of these stationary phases, coating different generations of dendritic moieties. For example, an efficiency value of 3,200 theoretical plates/m was obtained on a 10 m×0.25 mm i.d. column coated with the third generation dendronized sol-gel stationary phase. This corresponded to a minimum plate height of 0.31 mm and an optimum flow rate of 25 cm/s. Efficiency values on the order of only 1,000 pales/m were obtained on the columns coated with the related first and second generation stationary phases.

Based on this preliminary study, in which the dendronized reagent possessed simply benzyl ether termini and urea connectivity, it can be concluded that the dendritic architecture provides unique selectivity in capillary GC separations, and adds chromatographic and electro-migration separations to potential utilitarian purposes for dendrons. In view of the facile ability to create diverse useful canopies that can enshrine different specific functionality to achieve an appropriate molecular interaction and response event(s), installation of these complimentary supramolecular relationships for chromatographic interactions can lead to enhanced

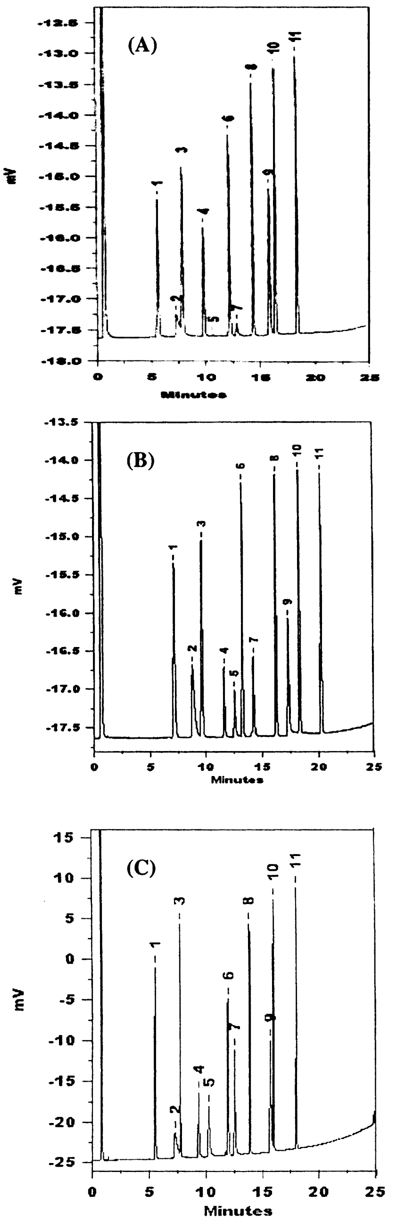


Figure 2. Chromatograms illustrating the GC separation of Grob test mixture on sol-gel dendrimer stationary phases with first (A), second (B), and third (C) generation benzyl-terminated dendritic material. Conditions: 100 m×0.25 mm i.d. fused silica capillary column; temperature programming from 40°C @ 6°C/min; helium as the carrier gas, 40 cm/s; split injection (100:1), 300°C; flame ionization detector, 350°C. Peaks: (1) *n*-decane; (2) 2,3-butanediol; (3) *n*-undecane; (4) 1-nonanal; (5) 1-octanol; (6) 2,6-dimethylaniline; (7) 2,6-dimethylphenol; (8) methyl decanoate; (9) dicyclohexylamine; (10) methyl undecanoate; (11) methyl dodecanoate.

selectivity in separations. The use of sol-gel chemistry to chemically bind these molecules to the capillary inner surface in the form of a stable organic–inorganic hybrid stationary phase coating opens new possibilities for enhanced performance and stability in differential migration separation techniques.

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References

1. Newkome, G. R.; Moorefield, C. N.; Vögtle, F. *Dendrimers and Dendrons*: *Concepts*, *Syntheses*, *Applications*; Wiley-VCH: Weinheim, Germany, 2001.
2. Narayanan, V. V.; Newkome, G. R. *Top. Curr. Chem.* **1998**, *197*, 19–77.
3. Newkome, G. R.; Moorefield, C. N. In *Comprehensive Supramolecular Chemistry*; Reinhoudt, D. N., Ed. Dendrimers; Pergamon: New York, 1996; pp. 777–832.
4. Smith, D. K.; Diederich, F. *Top. Curr. Chem.* **2000**, 183–227.
5. Zeng, F.; Zimmerman, S. C. *Chem. Rev.* **1997**, *97*, 1681–1712.
6. Jayaraman, N.; Nepogodiev, S. A.; Stoddart, J. F. *Carbohydr. Eur.* **1998**, 30–33.
7. Roy, R. S.; Das, K. *Chem. Commun.* **2000**, 519–529.
8. Aoi, K.; Itoh, K.; Okada, M. *Macromolecules* **1995**, *28*, 5391–5393.
9. Aoi, K. *Kobunshi* **1996**, *45*, 260.
10. Aoi, K.; Tsutsumiuchi, K.; Yamamoto, A.; Okabe, M. *Tetrahedron* **1997**, *53*, 15415–15427.
11. Aoi, K.; Tsutsumiuchi, K.; Yamamoto, A.; Okada, M. *Macromol. Rapid Commun.* **1998**, *19*, 5–9.
12. Newkome, G. R.; He, E.; Moorefield, C. N. *Chem. Rev.* **1999**, *99*, 1689–1746.
13. Astruc, D.; Blais, J.-C.; Cloutet, E.; Djakovitch, L.; Rigaut, S.; Ruiz, J.; Sartor, V.; Valério, C. *Top. Curr. Chem.* **2000**, *210*, 229–259.
14. Casado, C. M.; Cuadrado, I.; Morán, M.; Alonso, B.; Garcia, B.; González, B.; Losada, J. *Coord. Chem. Rev.* **1999**, *185–186*, 53–79.
15. Cuadrado, I.; Morán, M.; Losada, J.; Casado, C. M.; Pascual, C.; Alonso, B.; Lobete, F. In *Advances in Dendritic Macromolecules*; Newkome, G. R., Ed.; JAI: Greenwich, CT, 1996; pp. 151–195.
16. Cuadrado, I.; Morán, M.; Casado, C. M.; Alonso, B.; Losada, J. *Coord. Chem. Rev.* **1999**, *193–195*, 395–445.
17. Gorman, C. *Adv. Mater. (Weinheim, Fed. Repub. Ger.)* **1998**, *10*, 295–309.
18. Serroni, S.; Campagna, S.; Denti, G.; Juris, A.; Venturi, M.; Balzani, V. In *Advances in Dendritic Macromolecules*, *Advances in Dendritic Macromolecules*; Newkome, G. R., Ed.; JAI: Greenwich, CT, 1996; pp. 61–113.
19. Stoddart, F. J.; Welton, T. *Polyhedron* **1999**, *18*, 3575–3591.
20. Venturi, M.; Serroni, S.; Juris, A.; Campagna, S.; Balzani, V. *Top. Curr. Chem.* **1998**, *197*, 193–228.
21. Reetz, M. T. *J. Heterocycl. Chem.* **1998**, *35*, 1065–1073.
22. Bhyrappa, P.; Young, J. K.; Moore, J. S.; Suslick, K. S. *J. Am. Chem. Soc.* **1996**, *118*, 5708–5711.
23. Bhattacharya, S.; Dileep, P. V. *Tetrahedron Lett.* **1999**, *40*, 8167–8171.
24. Bhyrappa, P.; Young, J. K.; Moore, J. S. *J. Am. Chem. Soc.* **1996**, *118*, 5708–5711.

25. Köllner, C.; Pugin, B.; Togni, A. *J. Am. Chem. Soc.* **1998**, *120*, 10274–10275.
26. Köllner, C.; Schneider, R.; Togni, A. *Chimia* **1999**, *53*, No. 107.
27. Hierlemann, A.; Campbell, J. K.; Baker, L. A.; Crooks, R. M.; Ricco, A. J. *J. Am. Chem. Soc.* **1998**, *120*, 5323–5324.
28. Castagnola, M.; Cassiano, L.; Lupi, A.; Messana, I.; Patamia, M.; Rabino, R.; Rossetti, D. V.; Giardina, B. *J. Chromatogr. A* **1995**, *694*, 463–469.
29. Kuzdzal, S. A.; Monnig, C. A.; Newkome, G. R.; Moorefield, C. N. *J. Chem. Soc., Chem. Commun.* **1994**, 2139–2140.
30. Kuzdzal, S. A.; Monnig, C. A.; Newkome, G. R.; Moorefield, C. N. *J. Am. Chem. Soc.* **1997**, *119*, 2255–2261.
31. Muijselaar, P. G. H. M.; Claessens, H. A.; Cramers, C. A.; Jansen, J. F. G. A.; Meijer, E. W.; de Brabander-van den Berg, E. M. M.; van der Wal, S. *J. High Resolut. Chromatogr.* **1995**, *18*, 121–123.
32. Newkome, G. R.; Weis, C. D.; Childs, B. J. *Des. Monomers Polym.* **1997**, *1*, 3–14.
33. Newkome, G. R.; Weis, C. D.; Moorefield, C. N.; Fronczek, F. R. *Tetrahedron Lett.* **1997**, *38*, 7053–7056.
34. Newkome, G. R.; Weis, C. D. US Patent 5,703,271, 1997.
35. Newkome, G. R.; Weis, C. D. US Patent 5,773,551, 1998.
36. Newkome, G. R.; Moorefield, C. N. US Patent 5,886,126, 1999.
37. Newkome, G. R.; Moorefield, C. N. US Patent 5,886,127, 1999.
38. Newkome, G. R.; Weis, C. D. *Org. Prep. Proc. Int.* **1996**, *28*, 495–498.
39. Cardona, C. M.; McCarley, T. D.; Kaifer, A. E. *J. Org. Chem.* **2000**, *65*, 1857–1864.
40. Klausner, Y. S.; Bodansky, M. *Synthesis* **1972**, 453–463.
41. Wang, D.-X.; Chong, S.-L.; Malik, A. *Anal. Chem.* **1997**, *69*, 4566–4576.
42. Grob, K.; Grob, Jr., G.; Grob, K. *J. Chromatogr.* **1978**, *156*, 1–20.