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[9] The formation of π-allyl−Pd species by the insertion of methylenecyclopropanes into H−Pd bonds has been proposed to account for results of coupling reactions of methylenecyclopropanes with malonates or amines when catalyzed by a Pd complex; see N. Tsukada, A. Shibuya, I. Nakamura, Y. Yamamoto, *J. Am. Chem. Soc.* **1997**, *119*, 8123–8124.

[10] The reaction of a 1,3-diene with π-allyl−Pd complexes was also reported to cause formation of a C−C bond between a vinyl carbon atom of the diene and a sterically hindered π-allyl carbon atom of the complex; see R. P. Hughes, J. Powell, *J. Am. Chem. Soc.* **1972**, *94*, 7723–7732. Their results may be accounted for by assuming a 2,1-insertion of a double bond of butadiene into the more sterically hindered Pd−C bond of the π-allylpalladium complex, although they suggested another kind of mechanism at that time.

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Nematic Dendrimers Based on Carbosilazane Cores**

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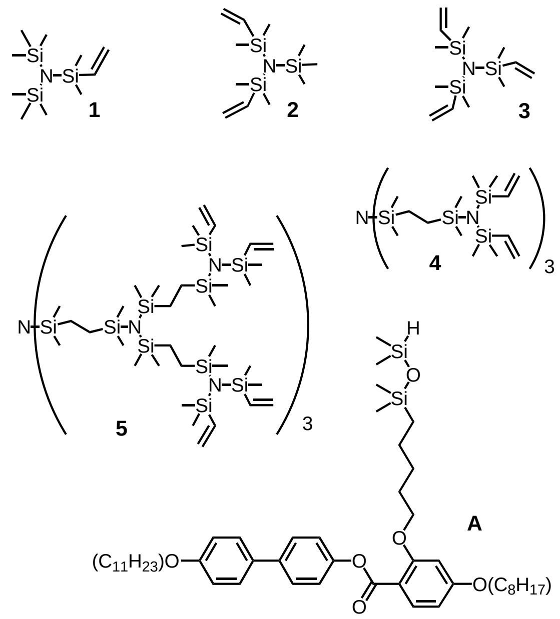
Research on dendritic liquid crystal systems has focused mainly on the investigation of materials that exhibit layered, columnar, cubic-phase structures.[1, 2] The emphasis has been associated with the chemical structure of these systems, in which a dendritic core and a periphery consisting of functional groups of different chemical composition, which are responsible for self-assembly processes, leads to nanoscopic phase segregation between core and periphery.[3, 4]

Thus, well-defined dendritic systems that exhibit nematic phase behavior and that are characterized only by orientational ordering and contain functional groups promoting nanophase separation have attracted considerable interest. The opposing forces of the nematic director field, which are attributed to the peripheral mesogens, and the tendency of the dendritic cores to undergo phase separation should lead to a new class of compounds with interesting properties in the liquid-crystalline (LC) state.[5]

This structural concept should allow the decoupling of the transition behavior and the ordering of the LC phase from the size of the molecules, which is a long-standing aim of LC polymer research. The materials should additionally be characterized by comparatively low viscosities.

The use of carbosilazane cores **1**–**5**, which display an overall threefold symmetry and possess a planar central core, allows the synthesis of microphase-separated systems.[6] The absence of nucleophilicity in the nitrogen atoms prevents complexation of ionic species in the dendritic core, which is detrimental for most electrooptic applications. Furthermore the use of these comparatively novel compounds, which are closer in structure to synthons applied in nonaqueous sol–gel synthesis of ceramic precursors than to conventional organic materials, is an attractive preparative challenge.



The synthesis of the dendritic and multipodal cores **3** to **5** has been reported earlier and is based on the reaction of the potassium salt of divinyltetramethyldisilazane (K[N{SiMe$_2$-vinyl}$_2$]) with chlorodimethylvinylsilane, which leads to the center of the dendritic system **3** (G_0).[6] Hydrosilylation of **3** with dimethylchlorosilane and the subsequent reaction with K[N{SiMe$_2$vinyl}$_2$] leads to compound **4** (G_1). Repetition of this divergent synthesis allows the preparation of compound **5** (G_2) and higher generation carbosilazane dendrimers, which bear functional vinyl groups at the periphery of the molecules. Compound **2**, which provides access to a dimeric system, was obtained by the reaction K[N{SiMe$_2$vinyl}$_2$] with trimethylchlorsilane. The carbosilazane **1**, which was synthesized to complete the homologous series, was obtained by the reaction

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[**] We acknowledge the EU for funding in the framework of the TMR network "Molecular Design of Functional Liquid Crystals" and thank the members of the network for the many helpful discussions.

of dimethylvinylchlorosilane with $K[N\{SiMe_3\}_2]$; thus the transition from monomeric to multipodal to dendritic systems can be investigated with this series of compounds.

The desired nematic phase behavior was achieved by using the mesogenic group **A**, whose synthesis has been reported previously.[7] The design of a mesogen such as **A** consisting of three aromatic rings connected by an ester group, flanked by terminal octyl and undecyl groups linked to the dendritic core through a short lateral spacer of five methylene groups and a 1,1,3,3-tetramethyldisiloxane group was judged to give the appropriate balance between coupling and flexibility and to be suitable to achieve nematic phase behavior close to ambient temperature and to avoid the occurrence of higher ordered LC phases.

A hydrosilylation reaction using Karstedt's catalyst in toluene was employed for the coupling of mesogens and dendritic cores.[8] To achieve complete reaction of the functional vinyl groups, the reaction mixture was kept between 40–45 °C; higher reaction temperatures led to the formation of by-products and the degradation of the catalyst, and lower reaction temperatures to incomplete conversion. The formation of the products was monitored by the disappearance of peaks at $\delta = 5.7$, 5.9, and 6.3 in the ^1H NMR spectrum (and at $\delta = 130.7$ and 143.6 in the ^{13}C NMR spectrum), which are associated with the vinyl groups, and the appearance of signals at $\delta = 0.4$ and 0.5 in ^1H NMR spectrum (and at $\delta = 10.1$ and 12.7 in the ^{13}C NMR spectrum), which are indicative of the formation of $CH_2{-}Si$ bonds. The final products were purified by column chromatography by using alumina (Brockmann II) as the stationary phase (the use of silica led to the cleavage of the Si–N bonds) and dichloromethane/hexane as eluent.[9] GPC analysis of the compounds **3A**, **4A**, and **5A** yielded values for the polydispersity ($\langle M_w\rangle/\langle M_n\rangle$) of 1.03 and smaller.

All of the final products show enantiotropic nematic phase behavior. Figure 1 shows a schematic representation of a dendritic molecule in the nematic phase. Polarized light transmission microscopy of these compounds is characterized by the immediate formation of typical nematic defect textures of low viscosity (a schlieren texture) with two and four brush defects ($s \pm ½$ and 1), as each material is cooled from the isotropic to the liquid crystalline state. The values for the transition temperatures, and the associated enthalpies and entropies for the second heating cycles obtained from differential scanning calorimetry (DSC) studies of each compound are listed in Table 1.

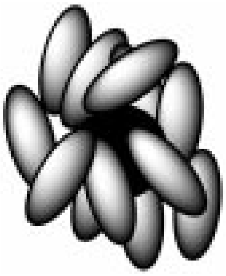

Figure 1. Schematic representation of a dendritic structure in the nematic phase.

The addition of the bulky carbosilazane group **1** to **A**, which results in **1A**, leads to the anticipated decrease of the stability range of the nematic phase from 38.5 °C for **A** to 18.7 °C for **1A** (Table 1). Increasing the number of side chains from one for **1A** to three for **3A** (G_0) leads to an expected increase in the isotropization temperature to 41.6 °C for **3A**; higher than that of the monomeric material **A** by 3.1 °C. The isotropization temperatures of the compounds **1A** (18.7 °C) and **2A** (36.5 °C), which are lower than that of **A** (38.5 °C), highlight that the formation of the nematic state is not favored in microphase-separated systems, when compared with smectic LC systems.[1, 2, 4]

Table 1. Transition temperatures as determined by DSC.[a]

Compound	Transitions [°C], {ΔH [J g^{-1}]}	$(\Delta S_{mol}/R)n^{-1}$
A	cr 17.0 N 38.5 {0.70} Iso	0.21
1A	cr −30.3 N 18.7 {0.31} Iso	0.13
2A	cr −12.6 N 36.5 {0.66} Iso	0.23
3A	T_g −26.0 N 41.6 {0.66} Iso	0.22
4A	T_g −23.0 N 40.1 {0.58} Iso	0.21
5A	T_g −22.3 N 40.9 {0.53 } Iso	0.20

[a] cr = crystalline, N = nematic, Iso = isotropic liquid, T_g = glass transition temperature [$(\Delta S_{mol}/R)n^{-1}$] normalized reduced transition entropy (n = number of mesogens).

A further increase of the size of the molecules from the generation G_0 compound **3A** to the dendritic generation G_1 compound **4A** and to the generation G_2 compound **5A** does not have a great influence on the isotropization temperature: 41.6 (**3A**), 40.1 (**4A**), and 40.9 °C (**5A**).

The low values for the transition enthalpies (ΔH) ranging from 0.31 to 0.71 J g^{-1} of this series, when compared to many other nematic systems, suggest the presence of low ordered systems. The values of 0.20–0.23 (exception **1A**) for the normalized isotropization entropy $(\Delta S/R)n^{-1}$ at the nematic to isotropic transition, are lower than those for smectic systems and are in line with the expected results for a less ordered LC phase. Interestingly, this change in entropy, which is related to the nematic ordering at the isotropization temperature, is almost independent of the size of the molecule whether it is a low molar mass material or a dendritic polymer. The lower value for entropic data of **1A** is attributed to the bulky carbosilazane group which impairs the nematic ordering.

These results indicate that the synthesis of these nanophase-structured nematic dendrimers leads to macromolecules with LC properties similar to those of comparable low molar mass compounds.

Received: December 11, 2000
Revised: February 28, 2001 [Z16254]

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[9] Compound **5** (150 mg, 6.1×10^{-5} mol) and compound **A** (1.3 g, 1.64×10^{-3} mol) were dissolved in dry toluene (10 mL). Fifteen drops of a solution of Karstedt's catalyst in xylenes (3.5%; Fluorochem) were added and the reaction mixture was stirred overnight at 45 °C. Volatiles were evaporated and the residue was purified by column chromatography on alumina (Brockmann II). The polarity of the eluent was varied from hexane/dichloromethane ratios of 3/1 to 1/3. Yield of isolated product: 60 mg (8%). ^{1}H NMR (399.7 MHz, $\mathrm{CD_2Cl_2}$, 25 °C): $\delta = 0.01$ (s, 144H; $\mathrm{-OSi(CH_3)_2-}$), 0.16–0.17 (5s (not resolved), 180H; $\mathrm{NSi(CH_3)_2-}$), 0.35–0.60 (m, 108H; $\mathrm{SiCH_2-}$), 0.88 (2t (not resolved), 72H; $\mathrm{-CH_3}$), 1.2–1.6 (m, $\mathrm{-CH_2-}$, 360H), 1.75–1.84 (m, 72H; $C\mathrm{\mathit{H}_2CH_2O}$), 4.00 (3t (not resolved), $\mathrm{-CH_2O}$), 6.51 (m, 24H; CH, (carbonyl)), 6.95, 7.20, 7.50, 7.56 (4d, 4 × 24H; CH, biphenyl unit), 7.98 (d, 12H; CH, (carbonyl)); ^{13}C NMR (100.4 MHz, $\mathrm{CD_2Cl_2}$, 25 °C): $\delta = -0.18$, 0.53 ($\mathrm{-Si(CH_3)_2O\text{-}Si(CH_3)_2-}$), 3.43, 3.50 ($\mathrm{-N\{Si(CH_3)_2\text{-}\}_2}$), 11.1, 12.7 ($\mathrm{NSi(Me)_2}\mathit{CH_2CH_2}\mathrm{\text{-}Si(Me)_2O-}$), 14.0 ($\mathrm{NSi(Me)_2}\mathit{CH_2CH_2}\mathrm{Si(Me)_2N-}$), 14.3 ($\mathrm{CH_3}$), 18.7 ($\mathit{CH_2}\mathrm{Si(Me)_2O}$), 23.1–32.3 ($\mathrm{-CH_2-}$), 68.5, 68.7, 69.3 ($\mathrm{-CH_2O}$), 100.5, 105.5, 111.6, 115.1, 122.6, 127.7, 128.3, 133.0, 134.5, 138.5, 150.6, 159.2, 161.9, 164.8 (C aromatic), 164.3 ($\mathrm{-\mathit{C}(O)O}$); GPC (THF, toluene standard) ($\langle M_w \rangle / \langle M_n \rangle = 1.024$).

Spin-Labeled Dendrimers in EPR Imaging with Low Molecular Weight Nitroxides

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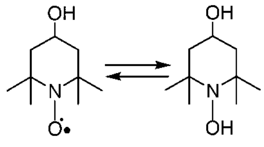
Electron paramagnetic resonance (EPR) imaging is an emerging technology that shows great promise in medical research applications for measuring free radical distribution, metabolism, and extent of oxygenation in tumors, organs and tissues.[1] However, the stable nitroxyl radicals (nitroxides) which these applications utilize, such as 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPOL), are prone to bioreduction to the analogous diamagnetic, EPR-silent hydroxylamines (i.e., TEMPOL-H; Scheme 1). The nitroxide and the hydroxylamine species rapidly establish an equilibrium that strongly favors the hydroxylamine in vivo.[2] Thus, the short half-life of nitroxides in vivo ($t_{1/2} \approx 3$ min) has limited further development and wide application of EPR imaging in the biomedical field.



TEMPOL TEMPOL-H

Scheme 1. The equilibrium established between TEMPOL and TEMPOL-H. The latter is favored in vivo.

Recently it was reported that intravenous injection of polynitroxyl-albumin (PNA) caused reoxidation of free hydroxylamine (shown to remain in the body for a relatively long period of time) back to the paramagnetic nitroxide.[3] This reagent has enabled high-resolution EPR imaging of rat heart and may also permit various therapeutic applications of nitroxides. Alternatively, polyamidoamine (PAMAM) Starburst™ dendrimers are spherical macromolecules which can be produced in successive generations, each with a specified and defined size and molecular weight as well as a high number of terminal primary amino groups.[4] Because of these characteristics and the low immunogenicity, PAMAMs are finding utility in a variety of applications, many of which are biomedical.[5] Due to their macromolecular nature, dendrimers are impermeable and when injected intravenously distribute primarily in the vascular space. This is in contrast to TEMPOL and TEMPOL-H, which are membrane permeable and move readily between the extra- and intracellular spaces, the latter being the major sites of nitroxide reduction.[6] Recently dendrimers labeled with 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) were used to evaluate the heterogenicity of their carbohydrate-substituted surfaces.[7a] Previous EPR studies of lower generation dendrimers with 2,2,5,5-tetramethylpyrrolidin-1-oxyl (PROXYL) conjugates have shown that the large spin–spin interaction encountered by dendrimer-labeled nitroxides causes extensive broadening of the EPR spectra, effectively making the latter indistinguishable from the base line.[7b] In contrast, the low molecular weight nitroxides exhibit sharp EPR spectra, and the intensities of the bands can be easily measured. Here we report the preparation and characterization of two novel spin-labeled dendrimers, a polynitroxyl G-6 PAMAM™ dendrimer with 198 (G-6-TEMPO-198) or with 80 (G-6-TEMPO-80) free TEMPO radicals on the surface of the macromolecule. We show that both dendrimers reoxidize TEMPOL-H back to its EPR-active form, TEMPOL, and therefore are potential TEMPO free radical, life-supporting agents for EPR imaging.

The commercially available G-6 PAMAM™ dendrimers are synthetic oblate spheroidal macromolecules composed of an ethylenediamine initiator core and repeating polyamidoamino units resulting in 256 amines on the surface. To attach TEMPO free radicals to the parent G-6 dendrimer, 4-amino-2,2,6,6-tetramethylpiperidine-1-oxyl (**1**, 4-amino-TEMPO) was first converted into 2,2,6,6-tetramethylpiperidine-1-oxyl-4-succinamic acid (**2**), which subsequently reacted to form the *N*-hydroxysuccinimidyl ester **3** (Scheme 2). Compounds **2** and **3** were characterized by their exact fast atom bombardment (FAB) mass spectra. No satisfactory elemental analyses could

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1433-7851/01/4014-2690 $ 17.50+.50/0