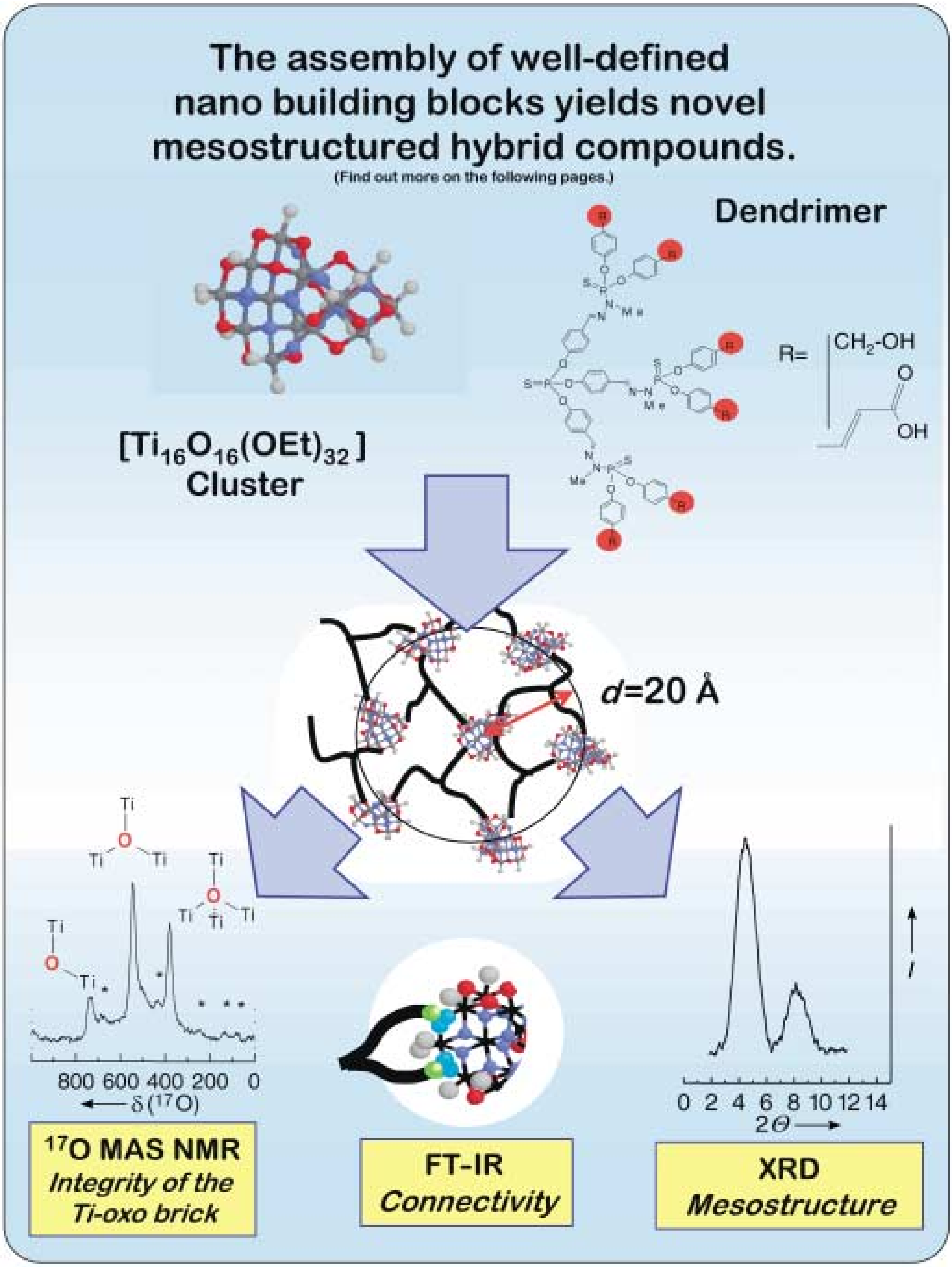

# The assembly of well-defined nano building blocks yields novel mesostructured hybrid compounds.

(Find out more on the following pages.)

$[Ti_{16}O_{16}(OEt)_{32}]$
Cluster

Dendrimer

$d$=20 Å

**$^{17}$O MAS NMR**
*Integrity of the Ti-oxo brick*

**FT-IR**
*Connectivity*

**XRD**
*Mesostructure*

# New Mesotextured Hybrid Materials Made from Assemblies of Dendrimers and Titanium(IV)-Oxo-Organo Clusters**

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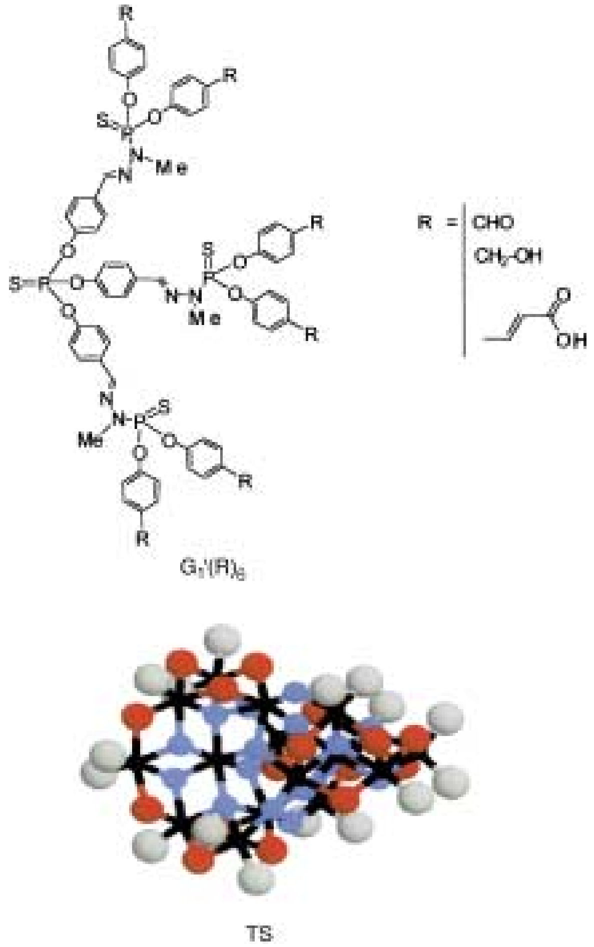
The discovery that micellar and lyotropic liquid-crystal phases can direct the assembly of periodic inorganic or hybrid organic–inorganic materials heralded a new class of materials with hierarchical structures and complex forms.[1] The chemical construction and patterning of such materials remains an important challenge in the science of organized matter chemistry.[1d] A number of imaginative routes to prepare new hybrid materials have been recently reviewed in some excellent articles.[2] The chemistry of silica-based hybrid systems is quite well understood and a large amount of work has been devoted to these materials, which have been formed as mesoscopic powders, films, and fibers.[3] On the contrary, the organic–inorganic interfaces built from non-silicate precursors (transition metals, Al or Sn) are more difficult to control; fine tuning of the hydrolysis/condensation and the assembly processes is more difficult to achieve. For many transition metals, their higher reactivity towards hydrolysis[4] precludes the reproducible synthesis of ordered hybrid phases. These problems can be overcome by resorting to less reactive, preformed transition metal–oxo building blocks and controlling their connection into organized nano- or mesostructures. Such strategies, based on the assembly of nano building blocks (ANBB)[5] with well-defined structures, can provide new pathways to design new chemical systems with novel properties or combinations of properties.

Herein we report, what is to the best of our knowledge, the first synthesis and characterization of new mesoscopically ordered hybrid materials built through the ANBB. New functional dendrimers[6] (hereafter called G1(COOH)$_6$ or G1(OH)$_6$; see Scheme 1) and structurally well-defined Ti-oxo-organo clusters, $[Ti_{16}O_{16}(OEt)_{32}]$[7–9] (TS, Scheme 1) were used as nano building blocks. The preparation of both building blocks (BBs) and the hybrids is described in the Experimental Section. Hybrids are named TS-G1(OH)$_6$-*Z* or TS-G1(COOH)$_6$-*Z*, in which *Z* represents the cluster-to-dendrimer molar ratio, TS/G1, with $0.25 < Z < 4$.



Scheme 1. Representation of the organic and inorganic building blocks: dendrimers $G_1'(CH_2OH)_6 = G1(OH)_6$, $G_1'(CH_2CH=CHCOOH)_6 = G1(COOH)_6$, and $G_1'(CHO)_6 = G1(CHO)$ (top) and TS (bottom). For TS the Ti cations are represented in black, $\mu_n$-O groups in blue, and the EtO groups in red (bridging) or white (terminal).

Upon mixing colorless solutions of TS and dendrimer G1(OH)$_6$ or G1(COOH)$_6$ in THF, a deep yellow sol is obtained. This color becomes more intense as the solvent evaporates and yellow-orange glassy solids are finally obtained after solvent removal (the color is more pronounced for TS-G1(COOH)$_6$-*Z* than TS-G1(OH)$_6$-*Z*). The original organic conjugate system shows an intense $\pi \rightarrow \pi^*$ absorption at 325 nm; the complexation to Ti(IV) centers gives rise to a bathochromic shift of about 40 nm.[10] The GC analysis performed on the cold-trapped solvent evaporated from the TS-G1(COOH)$_6$-*Z* systems shows the presence of ethanol, the quantity of which increases with the value of *Z*. The number of ethanol molecules released by the cluster is, in all cases, lower than the total number of acidic functions added. This suggests that the TS skeleton is not destroyed. Moreover, we note that the cluster is linked to between three to five acidic functions. Once obtained, the solids are insoluble in organic solvents such as THF or toluene. Yellow gels can also be obtained within 1 h when more concentrated solutions ($[TS] \approx 50$ mM) are kept in a closed vessel. All these results

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are consistent with the occurrence of nucleophilic reactions between the functional tips of the dendrimers and the titanium centers of the TS clusters. Ultimately a network of titanium-oxo-organo clusters, cross-linked through functional dendrimers forms. The key features, which are the control of the hybrid interface between the organic template and the inorganic building unit, the preservation of the $Ti_{16}O_{16}$ oxo core, and the mesotexturation of the resulting hybrid are discussed below.

Titanium alkoxides are known to be prone to very fast transalcoholysis reactions,[11] as has been shown through $^{47,49}Ti$ NMR spectroscopy.[12] Such reactions were also reported to occur with titanium oxo–alkoxo clusters, such as $[Ti_{16}O_{16}(OEt)_{32}]$; it has been shown that the titanium–oxo cores of these clusters are preserved in the presence of alcohols.[8, 9, 13] In the present work, similar transalcoholysis reactions occur between the ethoxy groups of the cluster and the benzyl alcoholic groups of the dendrimers tips, to lead to the formation of the TS-G1(OH)$_6$ hybrid materials. In the solid state, the covalent bonding between the dendrimers and the TS clusters was shown by $^{13}C$ NMR MAS (MAS = magic angle spinning) experiments, these show a new resonance signal at $\delta = 66.2$, which corresponds to the benzylic carbon of a $C_6H_5$-$CH_2$-O-Ti group. The integrity of the titanium–oxo core in the final hybrid solid was checked through solid-state $^{17}O$ NMR spectroscopic measurements on clusters that were selectively $^{17}O$ enriched in the oxo bridges.[8, 9, 13, 14] Figure 1a shows the typical $^{17}O$ NMR solid-state spectrum of enriched crystalline TS. Solid-state $^{17}O$ NMR spectrum of a typical dry TS-G1(OH)$_6$ hybrid ($Z = 0.4$, Figure 1b) exhibits three sets of resonance signals located at $\delta = 734$, 542, and 377, corresponding to the $\mu_2$-O, $\mu_3$-O, and $\mu_4$-O oxo species present in the TS cluster.[13] There is a significant peak broadening compared to the crystalline TS, which indicates a loss of symmetry. The chemical environments of the titanium–oxo ligands suffer subtle changes upon the interaction of the clusters with the dendrimers, leading to a distribution of sites. These results confirm that the $Ti_{16}O_{16}$ titanium–oxo core is conserved in the presence of mildly nucleophilic species, such as the alcoholic tips of the G1(OH)$_6$ dendrimers.

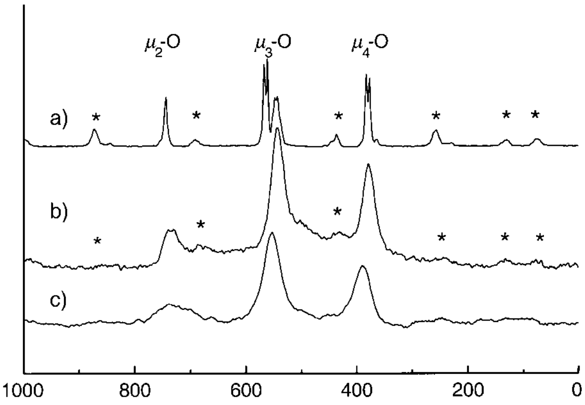


Figure 1. $^{17}O$ MAS NMR spectra recorded at $\nu(^{17}O) = 40.67$ MHz (spin rate 12.5 kHz) of a) TS particles and the b) TS-G1(OH)$_6$ ($Z = 0.4$), and c) TS-G1(COOH)$_6$ ($Z = 4$) hybrids. The asterisks denote rotation bands. The oxo resonances are indicated.

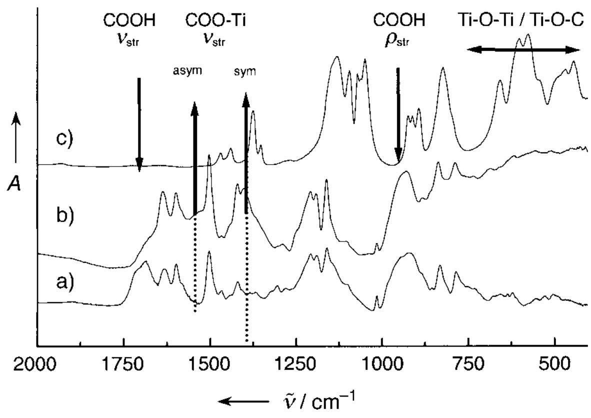


Figure 2. FT-IR spectra for the different BBs and hybrid systems: a) G1(COOH)$_6$ dendrimer; b) TS-G1(COOH)$_6$ ($Z = 2$); and c) the TS cluster. The most significant peaks are labeled.

FT-IR spectroscopy is a sensitive tool with which to monitor the reaction of the G1(COOH)$_6$ dendrimers and TS. The most important bands of G1(COOH)$_6$ (Figure 2a) are located at 921 (COOH dimer, out of plane stretching $\rho_{str}$ and $\nu_{P-O}$) and 1687 cm$^{-1}$ ($\nu_{C=O}$ of an $\alpha,\beta$ unsaturated acid[15]). The TS clusters display characteristic sharp $\nu_{Ti-OR}$ bands in the 400–750 cm$^{-1}$ region, as well as a broad absorption arising from the $\delta_{Ti-O-Ti}$ modes, as shown in Figure 2c. The $\nu_{TiO-C}$ vibrations of the surface ethoxy groups are also present (1049, 1076, 1094, and 1129 cm$^{-1}$).[11] These bands decrease in the spectra of the hybrid compounds (Figure 2b), which exhibit all the bands expected for the inorganic and dendritic species. The strong absorption of the dendrimer dominates this region. There are though, drastic changes upon TS addition for the bands arising from the carboxylate dendrimer (921 and 1687 cm$^{-1}$), which weaken in systems with increasing quantities of TS; the $\nu_{C=O}$ absorption corresponding to acidic tips in fact disappears when $Z = 2$; these results agree well with the GC results (see above). At the same time, two bands appear at 1402 and 1541 cm$^{-1}$ and their intensity increases with $Z$, although their observation is hindered by the strong dendrimer C–H signals. The reported positions are characteristic of the symmetric and asymmetric vibrations of bridging coordinated carboxylate species,[16] as is the band splitting of $\Delta\nu = 139$ cm$^{-1}$ which has been reported in many Ti–carboxylates.[17–19] The appearance of this band from a bridging carboxylate group, coupled with the loss of the peaks typical for the acidic dendrimer is evidence of the formation of the hybrid interface by Ti-O:C:O-Ti bonds. The $^{13}C$ NMR spectra of the hybrid systems (e.g. TS-G1(COOH)$_6$ z = 0.25, not shown) shows less-intense resonance signals ($\delta = 172$) for the carboxylate groups than observed for the dendrimer alone. At the same time, a resonance appears at $\delta = 168$ which is assigned to coordinated carboxylate units. Moreover, the presence of the remaining surface EtO groups belonging to TS clusters (not clearly seen in the IR spectra) is confirmed by the resonance signals at $\delta = 71$ and 72 (for TS-O-$CH_2$-$CH_3$) and $\delta = 18$ (for TS-O-$CH_2$-$CH_3$). Based on the collected NMR and FT-IR spectroscopic evidence, we can postulate that a fraction of the bridging EtO moieties is removed by the attack of the carboxylate dendrimer tips; in this way, nucleophilic substitution coupled to a single proton transfer from the acid to the alcohol suffices to substitute two coordination positions in vicinal Ti atoms. The integrity of the $Ti_{16}O_{16}$ inorganic core was also demonstrated through $^{17}O$ NMR spectroscopy (Figure 1c). The characteristic three sets of broad resonance signals ($\mu_n$-O oxo-species) of the cross-linked TS clusters appears for the TS-$G1(COOH)_6$-4 system. When the $Z$ ratio is decreased, further broadening of these resonance signals is observed, indicating that for higher carboxylate:titanium ratios ($Z < 0.1$) a fraction of the $Ti_{16}O_{16}$ cores is cleaved.

To understand the reactions involved in the first steps solution $^{17}O$ NMR spectroscopic experiments were performed on the initial mixtures. TS–AcOH (Ac = acetyl) model systems were studied to assess the behavior of the TS cluster surface towards a relatively strong nucleophile. $^{17}O$ NMR spectra measured in a TS:toluene solution[20] show that the main resonance signals of the $Ti_{16}O_{16}$ core ($\mu_2$-O $\delta = 750$; $\mu_3$-O $\delta = 563$ and 555; $\mu_4$-O$\delta = 383$) are slightly modified upon addition of small amounts of acetic acid ($H$ = [-COOH]:[TS] ratio $< 8$); all the signals undergo a slight broadening. A decrease in intensity of the $\mu_3$-O ($\delta = 563$) resonance is also observed. This change is in conjunction with the appearance of a new $\mu_3$-O resonance signal ($\delta = 565$) which indicates that the early substitution of ethoxy groups by acetato ligands occurs at some specific sites of the cluster. For a higher amount of acetic acid ($H > 8$), a fast cleavage of the $Ti_{16}O_{16}$ core is observed. In the case of TS-$G1(COOH)_6$ systems, all the characteristic resonances of the $\mu_n$-OTi units in the TS cluster ($n = 2$, 3, 4) are still observed by solution $^{17}O$ NMR spectroscopy, although an appreciable signal broadening for low $Z$ ratios can be seen. This feature is also associated with a decrease in the overall intensity of the NMR signal. Both effects are in fact typical of systems for which gelation processes take place; in this case, gelation is caused by the quick cross-linking of the clusters by the polyfunctional dendrimers. An increase in the molecular size of species probed by NMR spectroscopy can lead to broadening of the resonances and even a partial loss of the signal intensity.[21, 22] However, solid-state $^{17}O$ NMR spectroscopy of the final dry TS-$G1(COOH)_6$ hybrids shows that the cluster signature remains even for $Z = 0.25$ hybrid systems, which correspond to $H = 24$. For such a high acid to cluster ratio, and in the presence of small monofunctional organic acids such as HAcO, TS is destroyed. The rigid medium quickly attained in our cross-linked systems kinetically hinders the cleavage of the $Ti_{16}O_{16}$ core.

Diffractograms for TS-G1 hybrids were obtained using graphite-filtered $Cu_{K\alpha}$ radiation ($\lambda = 1.5406$ Å). The XRD patterns of the TS-$G1(OH)_6$ hybrids only exhibit one very broad diffraction peak at correlation distances ($d$ values) between 1.5–1.8 nm, indicating that a local order is attained: the higher the polymer contents, the higher the $d$ value. These distances are in agreement with the mean diameter of the Ti–oxo core.[23] For TS-$G1(COOH)_6$ systems, two diffraction lines are observed at lower two theta values (1.9 nm $< d <$ 2.1 nm), indicating a better degree of ordering (Figure 3); the ratio of the diffraction peaks is in the range 1.7–1.9 (Figure 3, inset). These lines are more intense for solids that are richer in TS because the inorganic building blocks have a higher scattering power. The correlation distances are greater for lower $Z$ values (see inset in Figure 3); this phenomenon also takes place in TS-$G1(OH)_6$ solids. This suggests that in both cases, the dendrimers act like spacers in the array of clusters. An analysis of the peak breadth by a simple Scherrer equation[24] allows an estimated coherent scattering domain (CSD)[25] of 5–6 nm in all cases. A local ordered array of TS clusters is thus formed in a volume of about 125 nm$^3$, that is, 2–3 times the correlation distance along each direction. The order blurs at longer distances. The symmetry of these arrangements cannot be ascertained, but the distances found could correspond to the [100] and [110] reflections of a closely packed arrangement. Noteworthy is that under our “dry” conditions, glasslike cluster–polymer hybrids are easily obtained with polymers (such as PEO-PPO-PEO, or PEO-$C_nH_{2n+1}$; PEO = poly(ethylene oxide), PPO = poly(propylene oxide) that can establish covalent interactions with the clusters. However, in the latter case, ordered phases are not obtained; XRD diagrams display flat patterns characteristic of amorphous hybrids. We can thus conclude that the symmetry of the organic template, as well as the ability of the cluster to anchor the dendrimer, are essential features in obtaining organized dispersions.

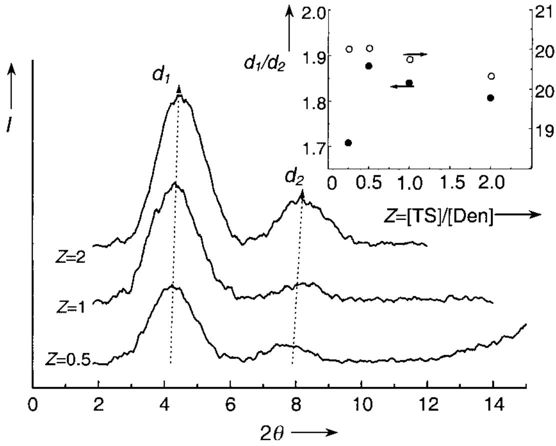
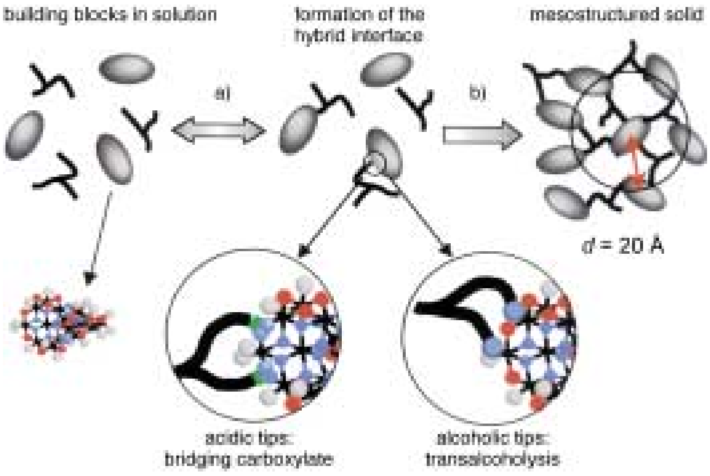


Figure 3. XRD diagrams for typical TS-$G1(COOH)_6$ phases; the particle to dendrimer ratio ($Z$) values are given in the Figure. Inset: variation of the distance ratios $d_1/d_2$ (closed dots) and the correlation distances, $d$ (open dots) with $Z$, for TS-$G1(COOH)_6$ phases.

New mesotextured hybrid materials comprising covalently bonded dendrimers and $[Ti_{16}O_{16}(OEt)_{32}]$ clusters can be easily synthesized by using preformed organic and inorganic building units. Moreover, the shape of the organic blocks dictates a pyramidal local symmetry, which is repeated to form a longer-range ordered texture. “Dry” synthesis conditions, as well as controlled polymer volume fractions (≈30–60%) hinder the formation of a continuous inorganic phase. The route to these TS-G1 hybrids (TS-$G1(COOH)_6$, TS-$G1(OH)_6$ with different $Z$ ratios) is sketched in Scheme 2, and is composed of three steps: 1) “snap-on” reactions at the surface level (in dilute solution), leading to hybrid bricks, 2) cross-linking of these hybrid moieties, spurred by solvent evaporation, 3) formation

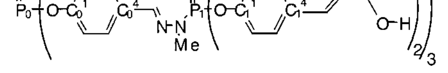


Scheme 2. Pictorial representation of the formation of the hybrid phase a) nucleophilic substitution; b) solvent evaporation; see text for full details.

of a bicontinuous hybrid gel, in which TS clusters are regularly spaced by the polymers. The combination of the surface chemistry of the clusters and the versatility of the dendrimeric tips permits these tailored phases.

## *Experimental Section*

Numbering for dendrimers G1(COOH)$_6$ (for G1(OH)$_6$, the numbering of the aromatic rings is the same):



G1(COOH)$_6$: A mixture of dendrimer G1(CHO)$_6$[26] (1423 mg, 1 mmol), malonic acid (1442 mg, 15 mmol), and piperidine (110 µL, 1.5 mmol) were heated at 95 °C in pyridine (15 mL) for 4 h and then refluxed for 15 min to complete carbon dioxide removal by using a routine Doebner-like procedure.[27] The yellow brownish solution was cooled in an ice bath and poured onto 10 M HCl (31 mL). The precipitate of dendrimer was then washed with water and dried under vacuum. The crude white powder was ultimately washed with diethylether and dried by evaporation to afford G1(COOH)$_6$ as an amorphous white powder, yield 93 %. $^{31}P\{^1H\}$ NMR ([D$_6$]DMSO):$\delta = 50.2$ (s, P$_0$), 61.0 (s, P$_1$); $^1H$ NMR ([D$_6$]DMSO):$\delta = 3.46$ (bd, $^3J_{H,P} = 10.0$ Hz, 9 H, P$_1$-N-CH$_3$), 6.58 (d, $^3J_{H,H_{trans}} = 17.1$ Hz, 6 H, C$_6$H$_4$-*CH*), 7.3–7.9 (m, 39 H, CH$_{arom}$ and CH=N), 7.65 (d, $^3J_{H',H_{trans}} = 17.1$ Hz, 6 H, *CH*-COOH), 12.3–12.8 (bs, 6 H, COOH); $^{13}C\{^1H\}$ NMR ([D$_6$]DMSO):$\delta =$ 34.6 (d, $^2J_{C,P_1} = 12.4$ Hz, P$_1$-N-CH$_3$), 121.0 (s, C$_6$H$_4$-*CH*), 123.0 (d, $^3J_{C,P_{1,0}} =$ 4.5 Hz, C$_{0,1}^2$), 130.2 (s, C$_0^3$), 131.5 (s, C$_1^3$), 133.3 (s, C$_1^4$), 134.3 (s, C$_0^4$), 142.4 (d, $^3J_{C,P_1} = 13.5$ Hz, CH=N-N-P$_1$), 144.3 (s, *CH*-COOH), 152.2 (d, $^2J_{C,P_0} =$ 7.5 Hz, C$_0^1$), 152.8 (bd, $^2J_{C,P_1} = 6.7$ Hz, C$_1^1$), 169.1 (s, COOH). IR (KBr):$\tilde{\nu} =$ : 1686 cm$^{-1}$ ($\nu_{C=O}$); elemental analysis calcd (%) for $C_{78}H_{66}N_6O_{21}P_4S_4$ (1675.56): C 55.91, H 3.97, N 5.01; found: C 56.05, H 3.89, N 4.93.

G1(OH)$_6$: BH$_3$ · SMe$_2$ (1.65 mL, 3.3 mmol, 2 M solution in CH$_2$Cl$_2$) was added to a solution of dendrimer G1(CHO)$_6$ (0.6 g, 0.422 mmol) in THF (20 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 4 h and then allowed to reach room temperature overnight. The sticky precipitate formed was dissolved with dry ethanol (1 mL) and the crude material was evaporated to dryness. The crude white foamy solid was washed with a mixture of pentane/ether (1/1, 50 mL) to afford G1(OH)$_6$ as a white powder, 98 % yield. $^{31}P\{^1H\}$ NMR ([D$_6$]DMSO):$\delta = 52.3$ (s, P$_0$), 62.6 (s, P$_1$); $^1H$ NMR ([D$_6$]DMSO): $\delta = 3.45$ (bd, $^3J_{H,P} = 10.6$ Hz, 9 H, P$_1$-N-CH$_3$), 4.57 (s, 12 H, CH$_2$), 5.25 (bs, 6 H, OH), 7.23–8.09 (m, 39 H, CH$_{arom}$ and CH=N); $^{13}C\{^1H\}$ NMR ([D$_6$]DMSO):$\delta = 33.2$ (d, $^2J_{C,P_1} = 11.9$ Hz, P$_1$-N-CH$_3$), 62.4 (s, CH$_2$), 120.7 (d, $^3J_{C,P_1} = 3.7$ Hz, C$_1^2$), 121.6 (bs, C$_0^2$), 128.0 (s, C$_1^3$), 128.7 (s, C$_0^3$), 133.0 (s, C$_0^4$), 139.9 (s, C$_1^4$), 140.4 (d, $^3J_{C,P_1} = 13.5$ Hz, CH=N-N-P$_1$), 148.9 (d, $^2J_{C,P_1} = 6.0$ Hz, C$_1^1$), 150.6 (bd, $^2J_{C,P_0} = 6.6$ Hz, C$_0^1$); elemental analysis calcd (%) for $C_{66}H_{66}N_6O_{15}P_4S_4$ (1435.43): C 55.23, H 4.63, N 5.85; found: C 55.39, H 4.72, N 5.79.

Hybrid materials were obtained using G1(COOH)$_6$ and G1(OH)$_6$ (carrying acidic or alcoholic ends respectively) and TS[7–9] both dissolved in THF, the concentrations were kept below $10^{-2}$ mol L$^{-1}$ to avoid the quick formation of a gel. The dissolved TS was added to the dendrimer in THF; this gave rise to orange-yellowish solutions. To avoid degradation of the [Ti$_{16}$O$_{16}$(OEt)$_{32}$] cluster the final solutions were placed in open vessels or Petri dishes into a desiccator under inert gas ($P_{H_2O} < 10$ ppm). After solvent removal, under nitrogen flow, transparent yellow, glassy solids are obtained.

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[23] TS can be considered an ellipsoid with a mean diameter (core plus ethoxy surface groups) of 17.5 Å; this estimation is based in the volume of the crystalline cluster, 5568 Å$^3$/cell (see ref [7b]). The approximate Ti–oxo core dimensions, taken as the maximum Ti$\cdots$Ti distance along the major and minor axis, are 10.8 and 7 Å, respectively.

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# Functionalized Fullerene as an Artificial Vector for Transfection

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Since our discovery that a photo-excited water-soluble fullerene oxidatively cuts the DNA duplex,[1] the interaction of organofullerenes with DNA has continued to attract the interest of chemists. Base-sequence-selective cutting has also been achieved with fullerene/DNA conjugates,[2] and a number of studies on structural variations of the reagent,[3] the mechanism of the photo cleavage,[4] and the applications to photodynamic therapy[5] have been reported. The lack of acute toxicity (LD$_{50} \gg 500\,\text{mg}\,\text{kg}^{-1}$) and the pharmacokinetics of oraganofullerene have been recorded.[6] We report herein an entirely new aspect of fullerene/DNA interaction, namely, the use of a functionalized fullerene as an agent for gene transfer (transfection). A newly designed "two-handed" fullerene (±)-**1** (see Figure 1) binds to duplex DNA, condenses it, and allows the complexed DNA to be delivered into and to be transiently expressed in the target cell.

The two-handed fullerene **1** is a unique amphiphile possessing [60]fullerene as the central core, on which a $C_2$-symmetric S-shape hydrocarbon structure, bearing two side chains, is attached. The basic $C_2$-core skeleton has been synthesized through the tether-directed regioselective double [3+2] cycloaddition by the route detailed in the Supporting Information.[7] The diamine side chains are separated by 1.2 nm from each other, they are protonated at pH 7,[8] and will exert strong electrostatic interactions with the parallel phosphate backbones of a DNA duplex (which, along the major groove, are also separated from each other by 1.2 nm). The phosphate charges on DNA will be neutralized at a reagent/base pair ratio ($R$) of 0.5. The central fullerene core provides a hydrophobic binding force for the condensation of DNA and probably also for the delivery of the fullerene/DNA complex to the interior of the target cell.

Various organic molecules have been developed for transfection,[9] and commercialized under a generic name of "lipofection" reagents such as Transfectam (**7**, also known as "DOGS", was used as the reference in these studies).[10] The central concept of lipofection is the conversion of a negatively charged DNA into a positively charged lipid-like entity through complexation with the reagent. Although these lipofection reagents have been extensively used in laboratories and in some cases in vivo,[11] the efficiency of transfection is by no means perfect and the reagents exhibit considerable cell toxicity, caused most likely through perturbation of the cell membrane by the lipophilic reagent. In designing a new strategy for gene delivery, we abandoned the idea of lipid mimicry and counted on the extremely high hydrophobicity of the fullerene core, with which the reagent/DNA complex may be delivered from aqueous medium into the cell.

For a given compound to act as a transfection vector, it must first bind tightly to DNA. In the absence of previous studies on a fullerene-based gene transfer approach, we needed to screen various molecules so that we could identify structural features necessary for tight DNA binding. To start the investigation, we synthesized the two-handed tetramine **1** as well as various related compounds **2**–**5** (Figure 1), each of which lacks some element of the structural features of **1**. The tetramine **2** lacks the fullerene core and the "one-handed" diamine **3** has only one cationic side chain. The dicarboxylic acid **4** is "two-handed", but is negatively charged in a neutral buffer solution. The affinities of these reagents for DNA duplexes were probed by several independent sets of experiments performed on calf thymus DNA, plasmid pBR322 DNA, and linear DNA fragments. The experiments were

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