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Published on Web 06/20/2006

Designer Dendrimers: Branched Oligosulfonimides with Controllable Molecular Architectures

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Abstract: The synthesis of "designer" dendrimers and dendrons with sulfonimide units at every branching point is reported. The synthesis is based on a series of (regio)selective functionalization reactions of amines and sulfonamides allowing precise control of the dendrimers' shape, the number of branches in each generation, and their peripheral decoration with functional groups. In principle, structurally different branches can be incorporated at any position within the dendrimer structure at will. Structurally perfect symmetrical and two-faced "Janus"-type dendrimers, as well as dendrimers and dendrons with intended interstices were synthesized on a preparative scale and fully characterized. Oligosulfonimide dendrons of various generations bearing an aryl bromide functional group at their focal points were attached to a *p*-phenylene core with the aid of Suzuki cross-coupling reactions resulting in dendrimers with photoactive terphenyl cores. The structure and the high purity of all dendritic sulfonimides were confirmed by means of ^{1}H and ^{13}C NMR, electrospray ionization mass spectrometry (ESI-MS), and elemental analysis. The utility of MALDI-TOF mass spectrometry for the analytical characterization of these dendrimers was evaluated in comparison to electrospray ionization. Two model branched oligosulfonimides were characterized in the solid state by single-crystal X-ray analysis. Reaction selectivities and conformation of sulfonimide branching points were rationalized by DFT calculations.

Introduction

Dendritic molecules (repeatedly multibranched species) currently encompass several groups of compounds. Among them are low molecular weight species such as dendrimers and dendrons[1] and macromolecular structures such as hyperbranched[2] and dendronized[3] polymers. Although the macromolecular dendritic species suffer from structural imperfections and polydispersity, they can be produced in one step and in large quantities, which is profitable for technological applications. Unlike the macromolecular dendritic structures, dendrimers can be prepared in a monodisperse, structurally perfect form by means of either covalent repetitive synthesis[4] or self-assembly.[5] Indeed, it is the perfect structural homogeneity that associated dendrimers with numerous biomedical applications, e.g., contrast agents and drug delivery agents.[6] However, gene transfection by polyamine dendrimers benefits from defects incorporated in the dendrimer structure so that it may be favorable to be able

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10.1021/ja061606b CCC: $33.50

to deliberately construct such nonperfect dendrimers.[7] The considerably large size and tunable peripheral functionality turns dendritic molecules to versatile building blocks for assembling larger nano- and mesoscopic hierarchical structures[8] that are of high interest for materials science. Consequently, because of this utility for basic and applied science, the main goal of dendrimer synthesis has been shifted from approaching an as large as possible number of generations to the rigorous control over their shape and selective (multi)functionalization. The architecture of a dendrimer can be controlled during or modified after the assembly of the dendrimer with the aid of selective reactions at the core, periphery, or internal layers. A selective peripheral functionalization of dendrimers is of paramount significance for regulation of stability, solubility, and multivalent functionality.

There are several options to synthesize dendritic molecules which combine the homogeneous interior with more than one type of peripheral functional group. For instance, covalently connecting two differently functionalized dendrons led to two-faced dendrimers,[9] while a statistical polyfunctionalization of polyamidoamines (PAMAM) with a mixture of acylating reagents resulted in a combinatorial dendrimer library.[10] Alternatively, selectively functionalized dendrimers and dendrons are obtained via a protection−deprotection strategy that often relies on statistical reactions requiring chromatographic separation of partially protected intermediates.[11] An intelligent choice of protective groups led to dendrimers bearing up to five different peripheral substituents.[12] Dendritic compounds in which each peripheral group is selectively bis-functionalized are obtained by either stepwise-selective reactions[13] or sequential combination of both selective and statistical reactions.[14] Besides selective peripheral functionalization, dendrimers can be specifically functionalized at the core[15] or at different layers.[16] The synthesis of dendrimers possessing nonsymmetrical architectures[17] also involves selective reactions and mixed approaches of protection−deprotection sequences and statistical reactions.

Here, we describe the synthesis of a new type of designer dendrimers and dendrons which carry sulfonimide units at every branching point. We show that the selectivity of the *N*,*N*-bis-sulfonylation (persulfonylation) of primary amines[14] together with repetitive methodology allows constructing selectively decorated and variably shaped dendritic oligosulfonimide structures from simple building blocks at will. The goal is to provide a set of easily accessible, rationally shapeable, and selectively functionalized dendritic platforms for challenging applications in science and technology. By utilizing the selectivities inherent in the reactions reported here, no complicated protective group strategy is required.

Results and Discussion

As mentioned in the Introduction, we have recently reported the partial functionalization, branching, and the preparation of dendrons from commercial oligoamines of the POPAM type by means of their peripheral persulfonylation.[14] The method, however, proved to be of limited use because, on one hand, it could only be applied for a peripheral decoration of branched oligoamines of the first generation and, on the other hand, the partial persulfonylation of the oligoamines was statistical, causing product separation difficulties. Having learned the limiting points of the peripheral decoration of the aliphatic polyamines, we began the current work: to employ the amine persulfonylation reaction, that is a 1→2 branching motif, in a repetitive synthesis that would lead to dendritic oligosulfonimides, a hitherto unknown type of oligobranched species. An important goal of this study is to test the reliability of the new repetitive procedures to achieve diverse dendritic structures. Consequently, in this work we arrive at third-generation (G3) oligosulfonimide dendrimers and dendrons of five different architectures.

The synthetic procedures are compiled in Schemes 1−5. The main reactions involved are *N*-sulfonylations and persulfonylations of amines, reductions of nitroaromatic compounds, and the Suzuki cross coupling (SCC). The arylsulfonyl chlorides used in this work were commercially available, highlighting to a large degree the synthetic accessibility and the potential structural versatility of dendritic oligosulfonimides. First, the schemes will be described in general terms and then addressed in more detail. Scheme 1 and Scheme 2 show the divergent synthesis of *N*-cored oligosulfonimide dendrimers possessing a defect-free, symmetrical structure (compound **4**) or structures with intentionally missing branches (compound **7**). Scheme 3 contains the synthesis of a two-faced, so-called Janus-den-

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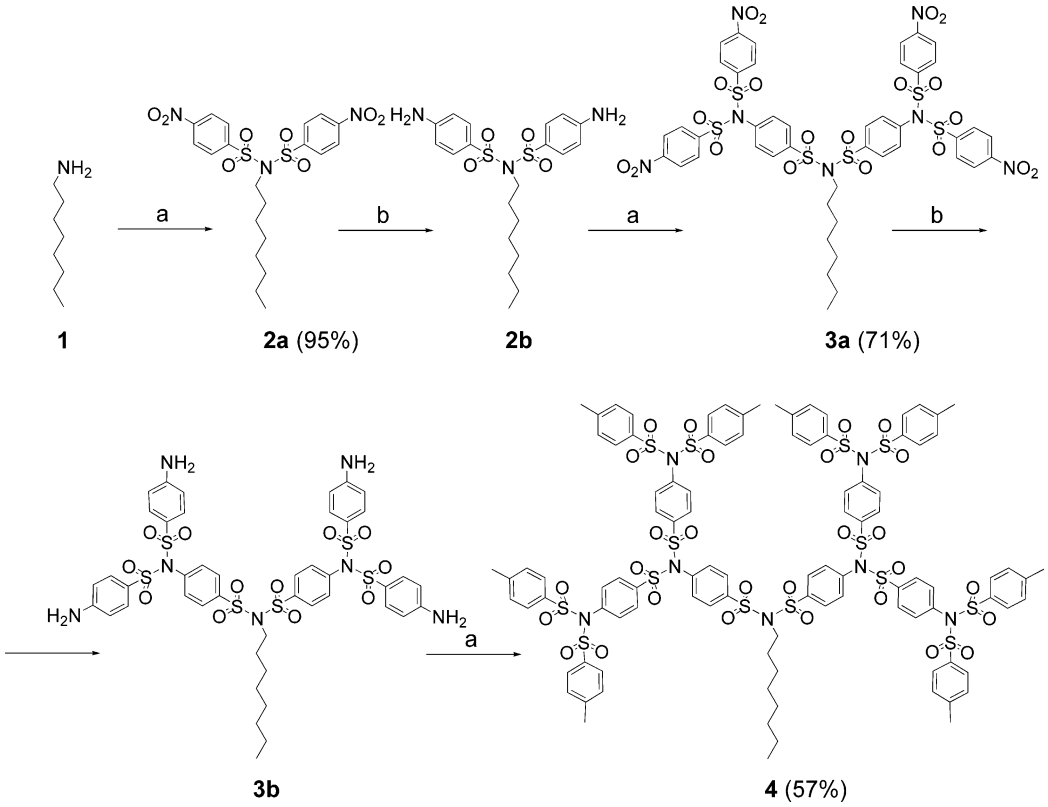
Scheme 1. Synthesis of Symmetrical Oligosulfonimide Dendrimers[a]



[a] Reagents and conditions: a) $ArSO_2Cl$, Et_3N, CH_2Cl_2, reflux; b) H_2, 10% Pd/C, C_6H_6/C_2H_5OH.

drimer[18] (compound **11**) demonstrating the possibility to use the intentional "defects" for the preparation of dendrimers with selectively functionalized peripheries. Scheme 4 illustrates the synthesis of oligosulfonimide dendrons **13**, **15**, and **17** bearing at their focal points aryl bromide functional groups. Scheme 5 depicts the convergent synthesis of terphenyl-cored dendrimers **18**, **19**, and **20**. A theoretical evaluation of the relative reactivities of amines and sulfonamides and the discussion on the geometrical features of branched sulfonimides on the basis of two single-crystal X-ray analyses are given after the synthetic part. Finally, the utility of ESI-FTICR and MALDI-TOF mass spectrometry for the characterization of the dendrimers under study is evaluated and compared.

Divergent Synthesis of Symmetrical *N*-Centered Oligosulfonimide Dendrimers. Scheme 1 outlines the synthesis of *N*-cored dendritic sulfonimides starting from *n*-octylamine **1**. The selection of the octylamine was envisaged by the optimal solubility/crystallinity balance of the *N*-octylsulfonimides as compared to those bearing shorter or longer alkyl chains.[19] Initially, the amine is one-step persulfonylated with an excess of *p*-nitrobenzenesulfonyl (nosyl) chloride in the presence of triethylamine, giving rise to the branched dinitro derivative **2a**. Compound **2a** is, in turn, catalytically reduced resulting quantitatively in diamine **2b**. Following the repetitive tactic, diamine **2b** is persulfonylated with nosyl chloride producing **3a** which is then reduced into tetraamine **3b**. The dendrimer growth is terminated via persulfonylation with a chemically inert arylsulfonyl chloride, in this case 4-methylbenzenesulfonyl (tosyl) chloride, yielding the octatosylate **4**. A noticeable advantage of the majority of oligosulfonimides reported in this work is that they can be efficiently purified by recrystallization. Taking into account an ample availability of different arylsulfonyl chlorides, this gives an opportunity for a fast preparation of the oligosulfonimide dendrimers decorated with the desired functional groups. Noteworthy, our new method of one-step persulfonylation of aliphatic amines by simply heating them in CH_2Cl_2 with about a 3-fold molar excess of both arylsulfonyl chloride and triethylamine affords much better yields and uses less expensive reagents than those in our former work[14] in which the reaction required long stirring with cesium carbonate in acetonitrile. The divergent synthesis of the symmetrical oligosulfonimide dendrimers shown in Scheme 1 is the simplest demonstration of the applicability of the persulfonylation reaction in the construction of repeatedly branched architectures. The following subsections disclose options of the rational shaping and selective decoration of dendritic oligosulfonimides.

Divergent Synthesis of *N*-Cored Oligosulfonimide Dendrimers with Planned Structural Interstices. The fact that the primary aliphatic amines can be persulfonylated in a stepwise-selective manner[14] allows preparing dendrimers bearing programmed structural defects. The synthetic pathway to these "defective" dendritic sulfonimides is illustrated in Scheme 2. Sulfonamide **5a** prepared from octylamine and nosyl chloride is reduced to *p*-aminobenzenesulfonamide **5b** which is, in turn, persulfonylated with nosyl chloride in the presence of triethylamine. If a large excess of nosyl chloride is used, the latter synthetic step yields a fully persulfonylated trinitro derivative

(18) The term "Janus" denoting two different faces of one entity is often used in dendrimer research. See for example refs 9c, 11b, and 11c.
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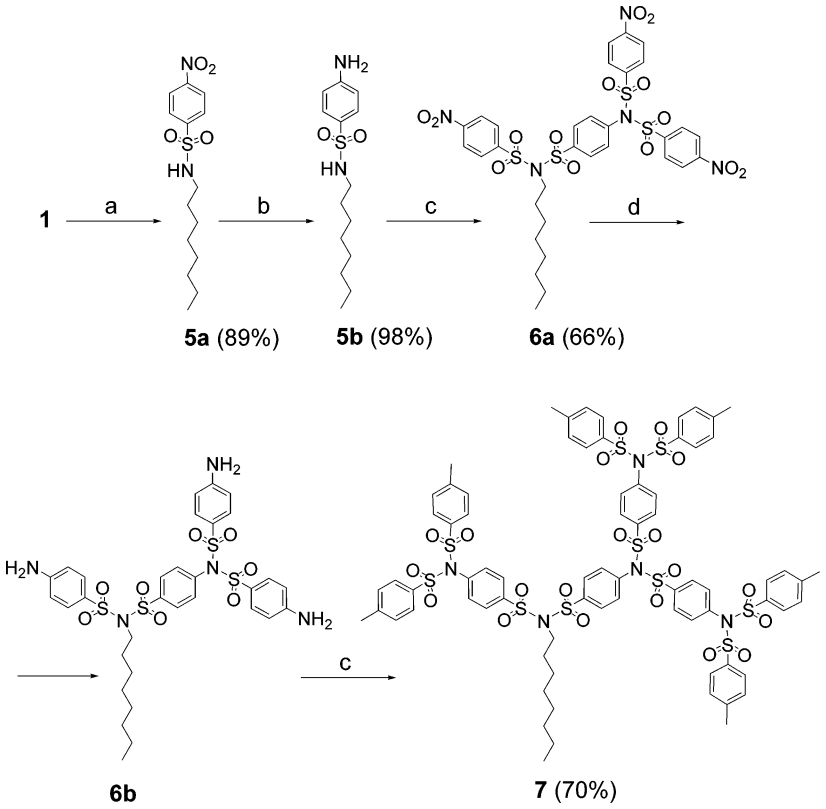
Scheme 2. Synthesis of Oligosulfonimide Dendrimers with Structural Interstices[a]



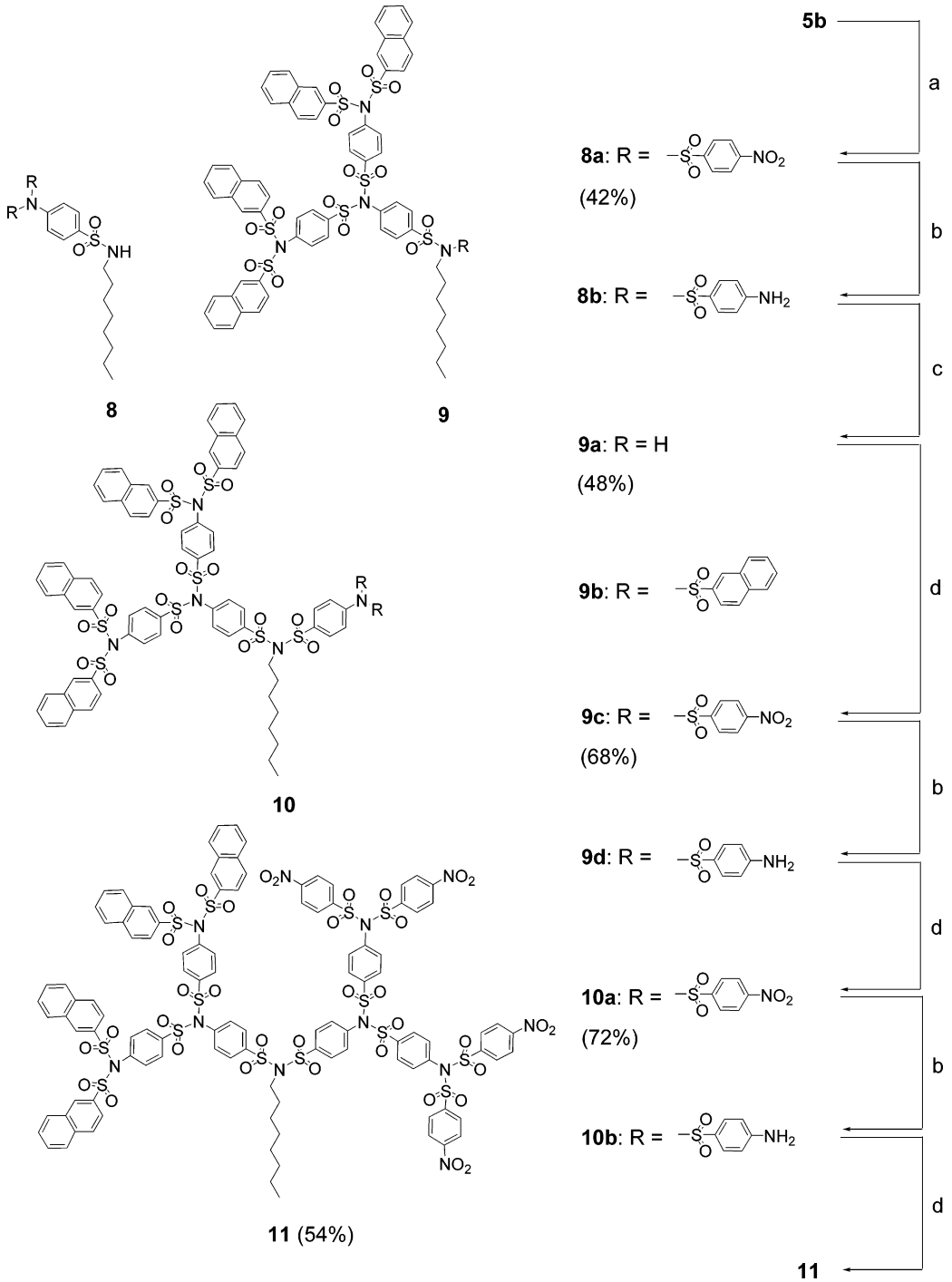
[a] Regents and conditions: a) 4-$NO_2C_6H_4SO_2Cl$, Et_3N, CH_2Cl_2, rt; b) $SnCl_2$, HCl, EtOH, reflux; c) $ArSO_2Cl$, Et_3N, CH_2Cl_2, reflux; d) H_2, 10% Pd/C, C_6H_6/C_2H_5OH.

6a. The beneficial side of this complete persulfonylation of the aminobenzenesulfonamide **5b** is that the nonsymmetric branched structure **6b** can be produced from the simple ambident aminosulfonamide in one step and used for the divergent growth of oligosulfonimide dendrimers with an intentional interstice. As demonstrated in Scheme 2, the trinitro derivative **6a** is reduced to the corresponding triamine **6b**, which after the consecutive persulfonylation with tosyl chloride gives rise to an unsymmetrical dendrimer **7**. The latter compound is a "defective" analogue of the structurally perfect dendrimer **4**, i.e., compound **7** is a result of an imaginary cutting of two branches off the 3rd generation of **4**. This type of *planned* introduction of structural asymmetries into dendritic structures is different from frequently occurring *unintended* incomplete conversions into higher generations during the synthesis. As will be shown below, even more sophisticated defects can be introduced into dendritic sulfonimides, e.g., a fully persulfonylated derivative **9b** in Scheme 3 can be considered as a "defective" dendrimer that lacks two branches of the second generation. It should further be noted that intermediate **5a** can be sulfonylated with a different sulfonyl chloride to yield a nonsymmetrically branched structure that can be used in further dendrimer synthesis. This reaction occurs in one step with an excess of sulfonyl chloride as described above. Treatment of **5a** under the same conditions will thus also lead to the corresponding sulfonimide. This permits us to introduce two different branches at inner dendrimer layers and control, for example, the distances between two branching points within the same generation (see below and Scheme 4).

Sequential Divergent Route to Two-Faced Oligosulfonimide Dendrimers (Janus Dendrimers). The possibility to choose between reaction at the arylamine or at the sulfonamide provides excellent flexibility for the synthesis of nonsymmetrical dendrimers via sequential growth of branches. As follows from Scheme 3, a selective persulfonylation of an aromatic amino group in **5b** enables the stepwise growth of branches. Treatment of *p*-aminosulfonamide **5b** with only two equivalents of nosyl chloride resulted in compound **8a** with the intact sulfonamide group. Compound **8a** is then reduced to diamine **8b** which is persulfonylated with four equivalents of 2-naphthyl sulfonyl chloride, yielding sulfonamide **9a**. Following the repetitive persulfonylation/reduction steps in Scheme 3 finally afforded the third generation Janus dendrimer **11**. A combination of the strategies shown in Schemes 2 and 3 in principle allows the dendrimer chemist to choose freely any branch as well as the substitution pattern at the periphery from the large variety of easily accessible aromatic sulfonyl chlorides. Of course, each asymmetry introduced at any branching point increases the number of synthetic steps necessary for a complete dendrimer synthesis, but even a dendritic structure in which all branches and endgroups are different could be made by this synthetic approach. In other words: starting with a desired structure of a sulfonimide dendrimer, a simple algorithm retrosynthetically converts it into the required sequence of suitable reaction steps.

Sulfonimide Dendrons with and without Structural Interstices and Their Use in Convergent Synthesis. The compounds discussed above are synthesized through a divergent procedure that usually has the disadvantage of considerable drops in yields as the dendrimer generation increases. To simplify the synthesis and to afford better yields of high-generation dendrimers, a convergent procedure is usually used. The convergent approach to dendritic structures is based on the

Scheme 3. Synthesis of Oligosulfonimide Dendrimers of Janus-Type[a]

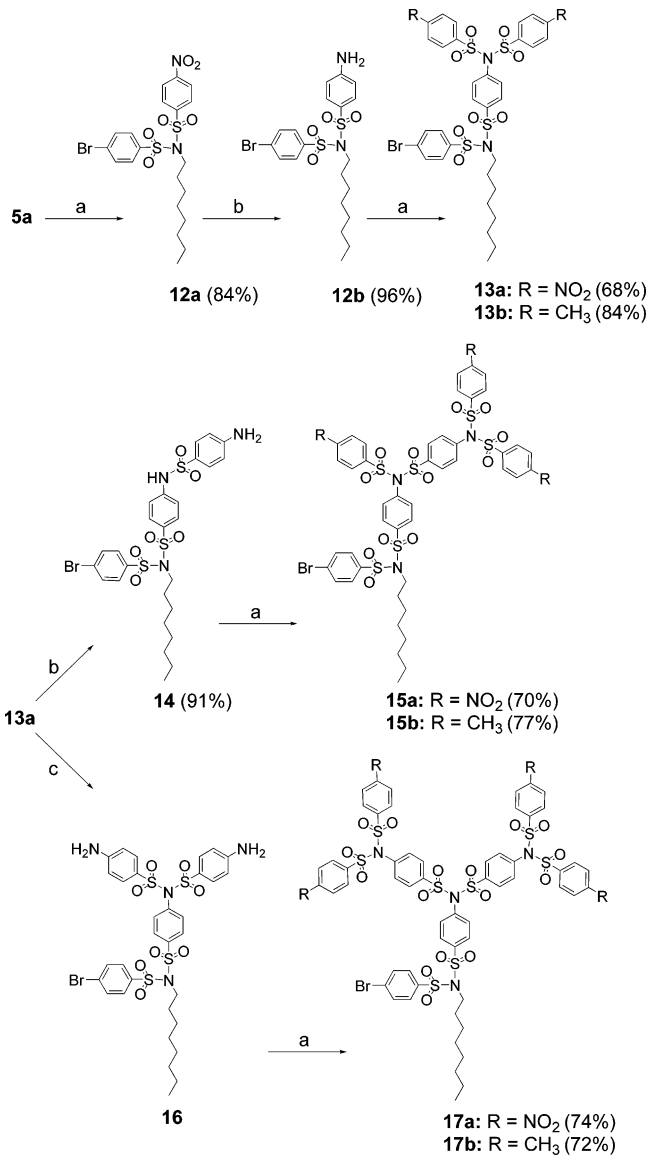


[a] Reagents and conditions: a) 2 equiv 4-$NO_2C_6H_4SO_2Cl$, Et_3N, CH_2Cl_2, reflux; b) H_2, 10% Pd/C, C_6H_6/C_2H_5OH; c) 4 equiv 2-$C_{10}H_7SO_2Cl$, CH_2Cl_2, reflux; d) 4-$NO_2C_6H_4SO_2Cl$, Et_3N, CH_2Cl_2, reflux.

preparation of dendrons, wedge-shaped branched compounds, bearing a single functional group at the focal point, and their covalent or supramolecular attachment to a multifunctional core. Consequently, a wide number of multifunctional compounds can be selected as potential cores for dendrimers. Given the stepwise selectivity of aliphatic amine persulfonylation and an easy access to functionalized arylsulfonyl chlorides, we designed sulfonimide dendrons.

The synthetic route to dendrons is shown in Scheme 4. The sulfonamide **5a** is persulfonylated with 4-bromobenzenesulfonyl chloride to yield sulfonimide **12a**. The latter carries the Ar−Br functional group that, on one hand, is stable toward the conditions of sulfonimide dendrimer synthesis and, on the other, can be used in metal-mediated cross-coupling reactions. As follows from Scheme 4, the nitro derivative **12a** is reduced to amine **12b** which is persulfonylated to corresponding derivatives **13a**, **b**. It has been found that **13b** can be transformed to two types of dendritic species, depending on the method chosen for the reduction of nitro groups. If the reduction of **13a** is performed in the $SnCl_2$/HCl system, it results in the splitting of one arylsulfonimide unit and gives rise to **14** as the sole product. As depicted in Scheme 4, the following persul-

Scheme 4. Synthesis of Oligosulfonimide Dendrons[a]

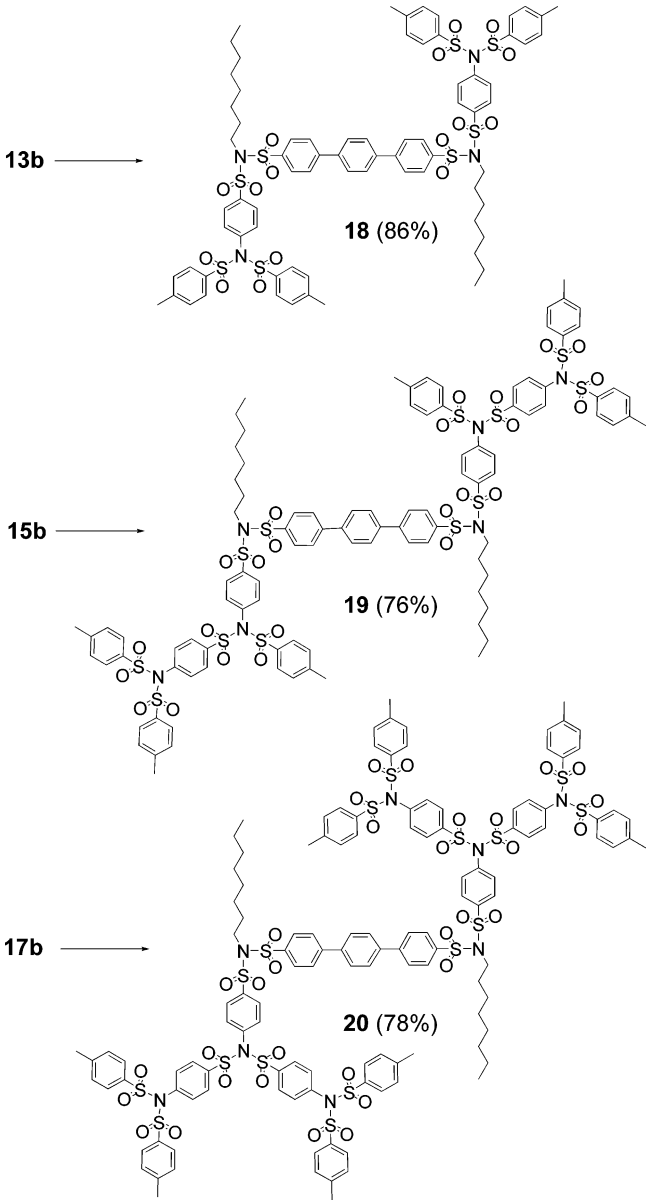


[a] Reagents and conditions: a) $ArSO_2Cl$, Et_3N, CH_2Cl_2, reflux; b) $SnCl_2$, HCl, EtOH, reflux; c) H_2, 10% Pd/C, C_6H_6/C_2H_5OH.

fonylation of **14** yields dendrons **15a**, **b** containing structural defects at their second generation as compared to **17a**, **b**. Consequently, not only is it possible to use different reactivities of amino and sulfonamide groups to construct nonsymmetric dendrimers, undesired branches can also be removed under the appropriate conditions—a reaction which is selective for sulfonimides. Otherwise, compound **13a** can be catalytically hydrogenated, producing diamine **16**. This is then persulfonylated, yielding symmetrical second generation dendrons **17a**, **b**.

Scheme 5 shows the use of the tosyl-decorated sulfonamide dendrons in the synthesis of terphenyl-centered dendrimers **18**–**20** via a double Suzuki cross-coupling reaction with 1,4-phenylene diboronic acid diester. Surprisingly, nitro compounds **13a**, **15a**, and **27a** do not react under the conditions of the Suzuki reaction. Since many different variants of cross-coupling reactions are available with different selectivities, the convergent synthesis described here is again a highly flexible approach to dendrimer synthesis.

Scheme 5. Synthesis of Terphenyl-Cored Oligosulfonimide Dendrimers[a]



[a] Reagents and conditions: 1,4-phenylene diboronic acid diester, Pd[(P(*p*-Tol)$_3$]$_3$, THF/H_2O, 80 °C, 24 h.

Theoretical Analysis of Relative Reactivities of Amines and Sulfonamides. During the syntheses described above, it became clear that **5b** first reacts one time with a sulfonyl chloride at its amino group. Under basic conditions, the second sulfonyl chloride again reacts at the same position, although a second sulfonamide is present in the molecule. Only when three equivalents of sulfonyl chloride were added, was full substitution to yield **6a** observed. This remarkable selectivity is easily explained qualitatively. From the point of view of an organic chemist, it is clear that the aryl amino group is the more nucleophilic position as compared to the sulfonamide whose lone pair at the nitrogen is delocalized in the amide bond. Consequently, the first reaction to yield the sulfonamide here is quite obvious. In the second step, one of the two sulfonamides needs to be deprotonated to create a center nucleophilic enough for the generation of a sulfonimide. The more acidic center is, of course, the aryl-substituted sulfonamide. The anion can be

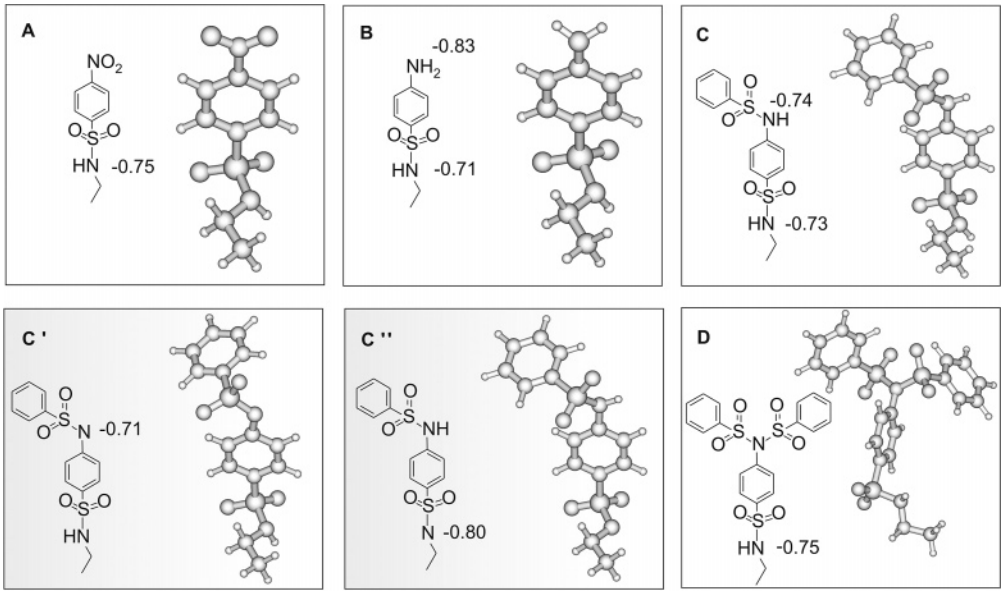


Figure 1. Six model structures optimized at the B3LYP/6-31G(d) level of theory and their molecular formulas. Numbers denote the electrostatic potential (ESP) charges of the nitrogen atoms.

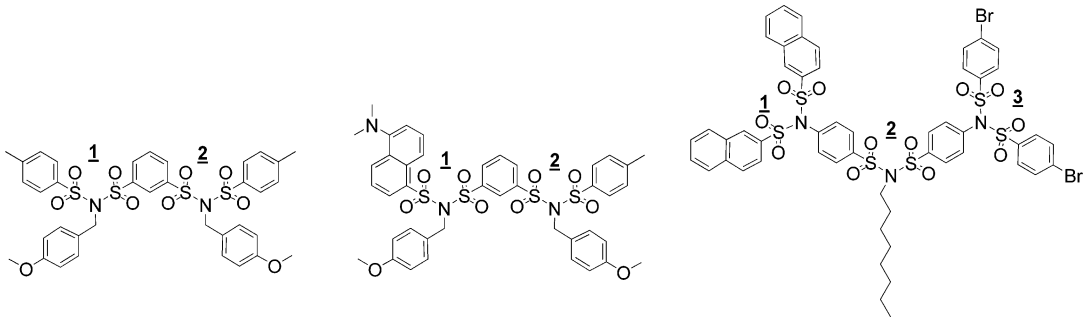
delocalized not only into the adjacent SO_2 group but also into the aromatic ring and the second SO_2 group. According to the vinylogy principle, this position is thus doubly activated. Therefore, the second substitution occurs at the same nitrogen as the first one. Finally, no other possibility exists for substitution at the remaining sulfonamide, when an excess of sulfonyl chloride is added.

To rationalize these synthetic findings in a quantitative way, we carried out ab initio calculations of four model structures A−D and the corresponding monoanions C′ and C″ as depicted in Figure 1. The geometries of these structures were fully optimized at B3LYP/6-31G(d) level of theory. The same theoretical level was applied to calculate atomic electrostatic potential (ESP) charges and vibrational frequencies in the optimized structures in the gas phase. Geometrical features of the sulfonimide branching point in the calculated structure D are discussed below in the context of crystallographic studies. The values of the negative ESP charges on nitrogen atoms are given in Figure 1 together with the optimized structures. The calculated values of the gas-phase vibrational frequencies for N−H bonds in substances A−D revealed no noticeable differences in their strengths, while the calculated ESP charges are good descriptors of the reactivity trends. A more negative charge at the arylamine nitrogen as compared to the sulfonamide nitrogen in substrate B indicates a higher nucleophilicity here. Therefore, the first equivalent of a sulfonyl chloride attacks the amino group of B and gives rise to an ambident intermediate C bearing two sulfonamide functional groups. Now, it is important to find the more acidic position at which a nucleophile is created more efficiently upon deprotonation. If one compares the two anions C′ and C″, a lower negative ESP charge is calculated for C′. This indicates a more efficient stabilization of the anion at the aryl-substituted sulfonamide and thus translates into higher acidity here. Structures D and A with single reactive unit each have similar ESP charges of their sulfonamide nitrogens and can finally be deprotonated in the presence of triethylamine at least to some extent. The use of an excess of the sulfonyl chloride causes the sulfonylation of the last reactive sulfonamide center in D and shifts the deprotonation equilibrium toward the anion. This is in agreement with the persulfonylation of **5a** with an excess of nosyl chloride yielding **6a** found in the experiment. To sum up, the calculated ESP charges give a good rationalization of the experimentally observed stepwise-selective persulfonylation of ambident substrates bearing both amine and sulfonamide functional groups.

Crystallographic Studies of Model Branched Sulfonimides. A detailed knowledge of the spatial arrangement of the dendrimer branches is very valuable because their optimum geometry determines the shape and functionality of the molecule. Ab initio calculations and molecular modeling may well provide some insight but are, of course, limited by the size of the molecules and the available conformational space. Also, solvent effects are usually not taken into account. X-ray crystallography usually affords the most direct description of a molecule's structural features. Due to the flexibility and fractal nature of dendrimers, their X-ray structural analysis is hampered by their low tendency to form suitable crystals; only a few successful examples were reported for first[20] and second generation[21] species. A Cambridge Structural Database search revealed that there is also a lack of reports on solid-state structures of neutral, nonconstrained sulfonimides. Available crystallographic studies include metal complexes of trifluoromethylsul-

(20) (a) Mekelburger, H.-B.; Rissanen, K.; Vögtle, F. *Chem. Ber*. **1993**, *126*, 1161−1169. (b) Lambert, J. B.; Pflug, J. L.; Denari, J. M. *Organometallics* **1996**, *15*, 615−625. (c) Kriesel, J. W.; König, S.; Freitas, M. A.; Marshall, A. G.; Leary, J. A.; Tilley, T. D. *J. Am. Chem. Soc*. **1998**, *120*, 12207−12215. (d) Larré, C.; Bressolles, D.; Turrin, C.; Donnadieu, B.; Caminade, A. M.; Majoral, J. P. *J. Am. Chem. Soc*. **1998**, *120*, 13070−13082. (e) Gossage, R. A.; Muñoz-Martinez, E.; Frey, H.; Burgath, A.; Lutz, M.; Spek, A. L.; van Koten, G. *Chem. Eur. J*. **1999**, *5*, 2191−2197. (f) Nanjo, M.; Sunaga, T.; Sekiguchi, A.; Horn, E. *Inorg. Chem. Commun*. **1999**, *2*, 203−206. (g) Ranganathan, D.; Kurur, S.; Gilardi, R.; Karle, I. L. *Biopolymers* **2000**, *54*, 289−295. (h) Brewis, M.; Clarkson, G. J.; Helliwell, M.; Holder, A. M.; McKeown, N. B. *Chem. Eur. J*. **2000**, *6*, 4630−4636. (i) Bauer, R. E.; Enkelmann, V.; Wiesler, U. M.; Berresheim, A. J.; Müllen, K. *Chem. Eur. J*. **2002**, *8*, 3858−3864. (j) Portner, K.; Nieger, M.; Vögtle, F. *Synlett* **2004**, 1167−1170. (k) Harder, S.; Meijboom, R.; Moss, J. R. *J. Oganomet. Chem*. **2004**, *689*, 1095−1101. (l) Saalfrank, R. W.; Deutscher, C.; Maid, H.; Ako, A. M.; Sperner, S.; Nakajima, T.; Bauer, W.; Hampel, F.; Hess, B. A.; van Eikema Hommes, N. J. R.; Puchta, R.; Heinemann, F. W. *Chem. Eur. J*. **2004**, *10*, 1899−1905. (m) Williams, A. A.; Day, B. S.; Kite, B. L.; McPherson, M. K.; Slebodnick, C. Morris, J. R.; Gandour, R. D. *Chem. Commun*. **2005**, 5053−5055.

Chart 1



21 **22** **23**

fonimide ligands[22] as well as alkylsulfonimide bridges incorporated into considerably constrained [2.2]paracyclophane structures.[23] Dendritic oligosulfonimides decorated with 4-nitrobenzenesulfonyl groups can be recrystallized from either chloroform or THF, producing amorphous colorless powders, whereas tosyl- and 2-naphthylsulfonyl-decorated oligosulfonimides precipitate from dichloromethane/methanol mixtures in the form of colorless, tiny, needle-shaped crystals. Although the purification of the branched oligosulfonimides is easily achieved by recrystallization, growing X-ray quality single crystals of the dendritic sulfonimides of second and third generations has thus far proved unsuccessful.

This prompted us to synthesize model branched sulfonimides **21** and **22** (Chart 1) possessing much better crystallinity compared to those in Schemes 1−5. Compounds **21** and **22** constitute a good set for studying the influences of symmetry and the nature of substutuents in branched oligosulfonimides. Diffraction quality crystals were grown from solvent mixtures of dichloromethane/hexane (**21**) and benzene/ethanol (**22**) using the vapor diffusion crystallization technique. The crystallographic data of these model oligosulfonimides are summarized in Table 1, while their molecular structures are depicted in Figure 2. The visual inspection of the solid-state structures points to a striking similarity of conformations of **21** and **22**. A clear transoid orientation of arylsulfonyl groups in both compounds is indicative of the true energetically favorable configuration of the unhindered sulfonimide branching points unlike the above-mentioned cisoid-type fixation of the sulfonimide bridge in the [2.2]paracyclophane.[23] The sulfonimide linkages in structure **23**[24] are arranged in a very similar way as those in **21** and **22**. Additional evidence for the energetically favorable arrangement of sulfonimide branches found in the crystalline state comes from the B3LYP/6-31G(d) optimized model structure D in Figure 1. Even though the calculations reflect the conformational preferences of the molecule in a vacuum, the configuration of the sulfonimide branching point in structure D is in excellent agreement with those found in compound **23** in the solid state. To compare the geometries of different sulfonimide branches in compounds **21**−**23** (Chart 1) and the calculated structure D (Figure 1), the values of dihedral angles $C_{ar}-S-N-S$ were extracted from their structural data. The data in Table 2 show that the values of the corresponding torsion angles do not vary significantly (by max 20°), which is indicative of restricted flexibility of the sulfonimide linkages. The configuration of the sulfonimide units seems to be insensitive toward different molecular symmetries, the nature of substituents, solvents, and the conditions used for crystallizations. Inclusion of benzene molecules into the crystal lattice of **22** (Figure 2c) also does not affect its conformation as compared to **21**, which crystallized without capturing solvent molecules. The similarity of the energetically favorable geometries of branching points in crystalline **21**−**23** and in a DFT optimized model structure D in a vacuum makes us confident that one can predict favorable conformations of the larger oligosulfonimide dendrimers.

Table 1. Crystallographic Data and Summary of Data Collection and Refinement for **21** and **22**

cmpd	**21**	**22**
formula	$C_{36}H_{36}N_2O_{10}S_4$	$C_{44}H_{44}N_3O_{10}S_4$
crystal system	orthorhombic	triclinic
space group	*Pbca*	$P\bar{1}$
a [Å]	19.8805(10)	6.9331(14)
b [Å]	11.7498(6)	18.493(2)
c [Å]	31.4557(15)	19.158(3)
α [deg]	90.00	114.416(13)
β [deg]	90.00	99.884(15)
γ [deg]	90.00	96.367(13)
V [Å^3]	7347.8(6)	2157.7(6)
Z	8	2
ρ [g cm^{-1}]	1.419	1.39
μ [mm^{-1}]	0.319	0.282
diffractometer	Xcalibur PX CCD	Xcalibur PX CCD
radiation	Mo Kα	Mo Kα
λ [Å]	0.71073	0.71073
T [K]	293	293
max 2*θ* [deg]	50	50
no. of data	49546	12122
no. of unique data	8460	4245
no. of unique data [$I > 2\sigma(I)$]	3383	2876
no. of variables	469	555
no. of restraints	170	0
$R(F)$ for $I > 2\sigma(I)$	0.0572	0.0679
w$R2(F^2)$ for all data	0.1217	0.1774
min/max diff. peak [e Å^{-3}]	−0.225/0.397	−0.171/0.214

(21) (a) Seyferth, D.; Son, D. Y.; Rheingold, A. L.; Ostrander, R. L. *Organometallics* **1994**, *13*, 2682−2690. (b) Rajca, A.; Janicki, S. *J. Org. Chem.* **1994**, *59*, 7099−7107. (c) Sekiguchi, A.; Nanjo, M.; Kabuto, C.; Sakurai, H. *J. Am. Chem. Soc.* **1995**, *117*, 4195−4196. (d) Karakaya, B.; Claussen, W.; Gessler, K.; Saenger, W.; Schlüter, A. D. *J. Am. Chem. Soc.* **1997**, *119*, 3296−3301. (e) Brewis, M.; Clarkson, G. J.; Goddard, V.; Helliwell, M.; Holder, A. M.; McKeown, N. B. *Angew. Chem.* **1998**, *110*, 1185−1187; *Angew. Chem., Int. Ed.* **1998**, *37*, 1092−1094.

(22) For example: Polyakov, O. G.; Ivanova, S. M.; Gaudinski, C. M.; Miller, S. M.; Anderson, O. P.; Strauss, S. H. *Organometallics* **1999**, *18*, 3769−3771.

(23) De Ridder, D. J. A.; Goubitz, K.; Fontijn, M.; Capkovà, P.; Dova, E.; Schenk, H. *Acta Crystallogr.* **2001**, *B57*, 780−790.

(24) Lukin, O.; Gramlich, V.; Shivanyuk, A. Preliminary data on single-crystal X-ray analysis. The crystals proved to be highly unstable and decomposed within minutes during irradiation. Although we could extract the approximate values of dihedral angles $C_{ar}-S-N-S$, more than 10 carbon atoms of the molecule and all of the entrapped chloroform solvent could not be located from the electron density map. Attempts at growing better crystals of **23** are in progress.

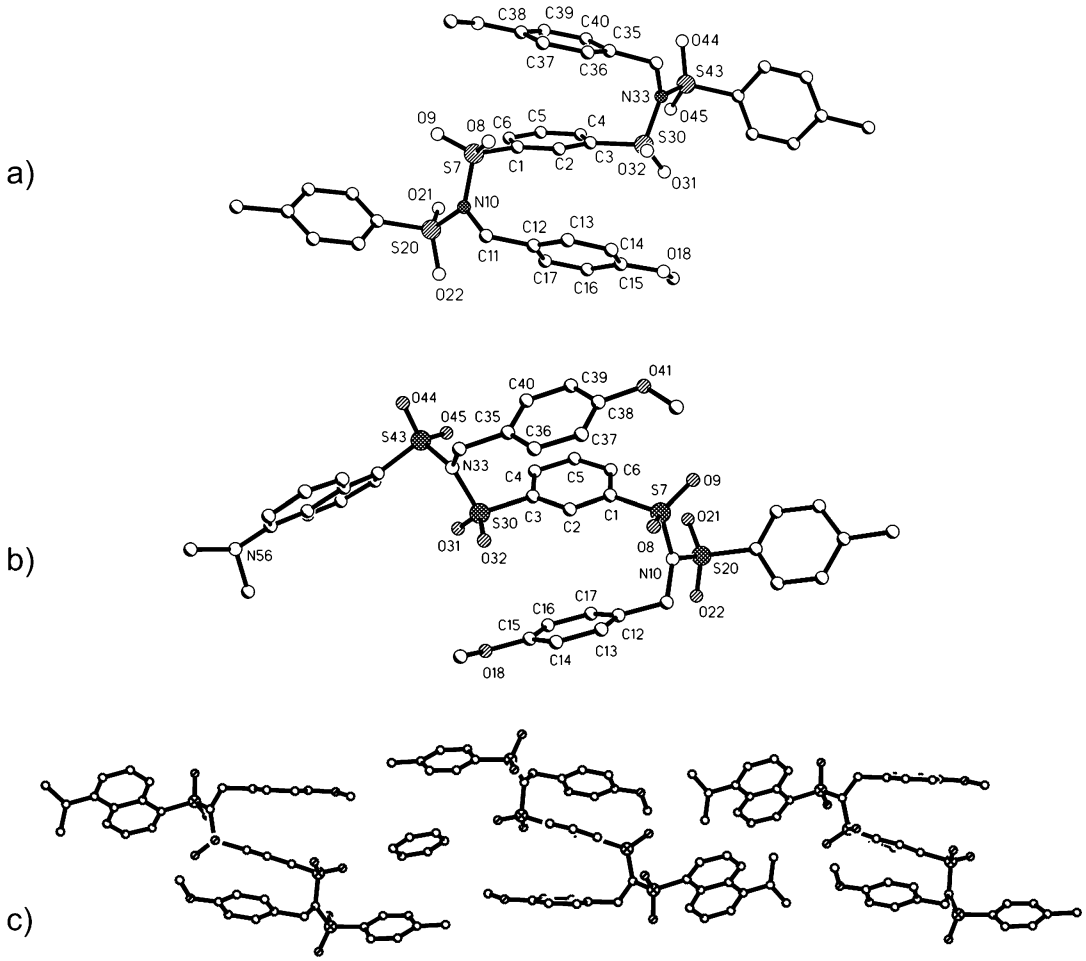


Figure 2. (a) X-ray molecular structure of **21**; (b) X-ray molecular structure of **22**; (c) packing of **22** in crystal.

Table 2. Values of $C_{Ar}-S-N-S$ Torsion Angles in Oligosulfonimides **21**−**23** (Chart 1) and D (Figure 1)

	branching point		
cmpd	1	2	3
21	79.9° 88.5°	84.6° 99.8°	−
22	64.6° 94.5°	77.7° 90.7°	−
23	69.4° 78.9°	79.5° 91.5°	68.9° 85.0°
D	83.9° 91.5°	−	−

Mass Spectrometric Study of Oligosulfonimide Dendrimers. Mass spectrometry is a particularly valuable method for the analytical characterization of dendrimers, because imperfections such as missing branches can immediately be detected due to their lower molecular masses. Quite often MALDI-TOF mass spectrometry is used, because this combination of ionization source and analyzer combines quite a large mass range with sufficient resolution. However, and particularly with sulfonamide and sulfonimide dendrimers, precaution is indicated when MALDI is used as the ionization method, because ionization artifacts are generated when acidic matrixes such as 2,5-dihydroxy benzoic acid (DHB) are used.[25] In the laser-heated matrix, sulfonimide groups are cleaved, and sulfonamides are generated. Consequently, the MALDI mass spectra seem to indicate incomplete substitution at the branching points. The ESI mass spectra, however, provided evidence for dendrimers of high purity, and thus the impurity signals in the MALDI spectra turned out to be ionization artifacts.

The dendrimers under study here have been characterized by both variants of mass spectrometry to examine the utility of the two ionization methods. Figure 3 (top) shows the ESI mass spectrum of nonsymmetric **9d** as a representative example. Protonation seems to be more difficult than attachment of background Na^+ or K^+, even though the spray solvent is methanol and the molecule bears an aniline moiety which should easily be protonated. This indicates an energetically favorable alkali cation binding—likely in an at least bidentate fashion through two sulfonyl oxygen atoms. In line with earlier results,[25a] the dendrimer forms ions with Na^+ ($m/z = 1532$) and K^+ ($m/z = 1548$). The ESI mass spectrum only shows a trace amount for a defect in which one peripheral branch was missing ($[X + Na^+]$ at $m/z = 1342$). This undesired defect can easily be removed by an additional recrystallization from CH_2Cl_2/CH_3OH. The MALDI mass spectrum (Figure 3, bottom; matrix: DHB) shows a completely different picture. The structurally perfect dendrimer appears with quite low intensity, whereas defects (in which up to all four terminal naphthylsulfonyl branches are replaced by protons) appear as quite intense signals

(25) (a) Felder, T.; Schalley, C. A.; Fakhrnabavi, H.; Lukin, O. *Chem. Eur. J.* **2005**, *11*, 5625−5636. (b) Baytekin, B.; Werner, N.; Luppertz, F.; Engeser, M.; Brüggemann, J.; Bitter, S.; Henkel, R.; Felder, T.; Schalley, C. A. *Int. J. Mass Spectrom.* **2006**, *249*−*250*, 138−148.

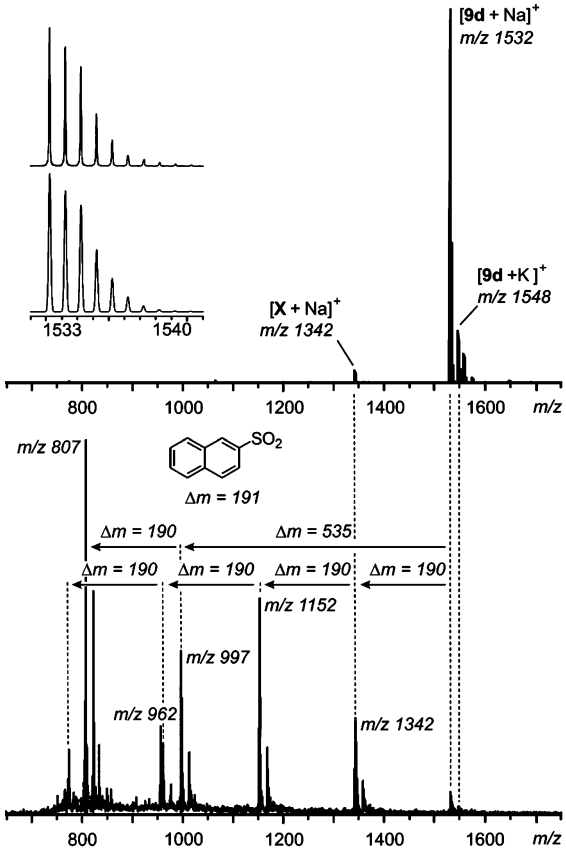
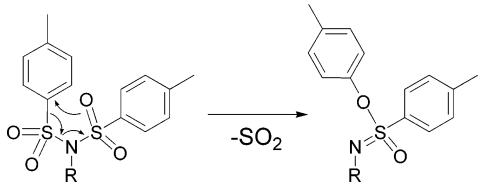


Figure 3. (Top trace) ESI-FTICR mass spectrum of a 50 μM methanol solution of **9d**. (Inset) Experimental isotope pattern (top) exactly matches the calculated one (bottom). (Bottom trace) MALDI mass spectrum of the same sample using 2,5-dihydroxy benzoic acid as the matrix.

with a repetitive spacing of $\Delta m = 190$ Da below the intact dendrimer ion. In addition, the signal at $\Delta m = 535$ Da below the parent ion corresponds to a whole missing first-generation dendron. The comparison of both mass spectrometric methods clearly leads to the conclusion that MALDI using DHB as the matrix is not suitable for characterizing the dendrimers under study with respect to their purity and to the absence or presence of defects in the sample. ESI mass spectrometry, in contrast, provides a very reliable analytical tool with which the dendrimers described here could easily be characterized.

In earlier reports, different isomeric defect structures could be distinguished with respect to their connectivities by MS/MS experiments.[24a] In similar experiments, mass-selected dendrimer ions were subjected to collisional activation which induces fragmentation in the gas phase. While it is not as easily possible to distinguish different structures of the dendrimers discussed here, they showed an interesting fragmentation channel not observed before. Besides 1,2-elimination reactions leading to the expulsion of C_8H_{16} from the alkyl chain at the focal point and besides cleavages of peripheral branches, signals for losses of SO_2 molecules also were observed even directly from the parent ions. A tentative mechanism by which this reaction could occur without any other neutral fragment is depicted in Scheme 6. Intramolecular ipso substitution proceeding through a favorable five-membered transition structure would lead to the loss of SO_2 in a concerted fragmentation reation while all other parts of the molecule remain connected to each other.

Scheme 6. Tentative Mechanism of the Loss of SO_2



While collision-induced fragmentations of mass-selected dendrimer ions in the gas phase do not yield sufficiently structure-sensitive mass spectra, the defects observed during MALDI ionization contain some structural information. In Figure 3 up to four naphthyl sulfonyl branches can be cleaved from the periphery. Consequently, at least a lower limit for the number of peripheral branches can be determined. Also, the loss of a G1 dendron is observed so that the presence of this subunit in the dendrimer structure can be deduced. Finally, the aminophenyl sulfonyl group at the focal point is not cleaved. This is likely due to the presence of an alkyl chain at the central sulfonimide nitrogen, which does not delocalize charges formed during the fragmentation reaction as efficiently as an aryl chain.

In conclusion, the combination of both mass spectrometric methods provides purity information (from ESI-MS) and some structural details (from MALDI-MS). It is thus advantageous to use both methods irrespective of the artifacts arising during ionization in the MALDI matrix.

Conclusions

The syntheses of a novel type of dendrimer are reported which use sulfonimides as the branching points in each generation. As reactants, arylsulfonyl chlorides can be used, a large variety of which are easily available either commercially or by a few simple synthetic steps. Due to the inherent reactivity trends for the single and double substitution of amines by sulfonyl chlorides, full control over the number of branches and their nature at each branching point can be exerted. Consequently, the sulfonimide dendrimers can be precisely designed with respect to their structural details and thus their shapes. In addition, undesired sulfonimides can be converted selectively into the corresponding sulfonamides, i.e., branches can selectively be removed. Finally, the divergent approach can be accompanied by a convergent one utilizing, for example, metal-catalyzed cross-coupling reactions. Many other substituents at the focal point (instead of the aryl bromides reported here) should offer many more possibilities to connect dendrons to many different core molecules. This synthetic approach thus offers a maximum degree of flexibility with the option to fully and precisely control the dendrimer architecture with respect to even individual branches or the well-defined attachment of particular functional groups at the periphery. It has the advantages of a large variety of easily available, inexpensive building blocks, the quite high chemical stability of sulfonimides, and a usually convenient purification of the products by recrystallization, making the production of multigram amounts straightforward. Finally, it allows the dendrimer chemist to use divergent or convergent methodology or, maybe most interesting, a combination of both.

Particularly interesting features from both structural and functional standpoints constitute double-faced "Janus"-type dendrimers and terphenyl-centered dendrimers. Thus, the den-

dritic sulfonimides reveal many advantages. A somewhat limiting step is that the dendrons bearing aryl bromide functional groups suffer from partial hydrodehalogenation during the Pd-catalyzed reduction step.

Our current goals involve (i) testing the generation limit of the oligosulfonimide dendrimers, (ii) crystallizing and performing single crystal X-ray analysis of larger dendritic oligosulfonimides, (iii) employing the selectively functionalized dendritic oligosulfonimides for construction of covalent and supramolecular structures of increased complexity.

Acknowledgment. We thank Prof. A. D. Schlüter (ETH Zurich) for his complete support and critical remarks for the manuscript. We are also grateful to Prof. F. Vögtle for stimulating discussion at initial stages of this work. The Zurich group acknowledges partial financial support from Swiss National Science Foundation (SNF, Grant Number 200021-111739). C.A.S. and T.F. acknowledge the Deutsche Forschungsgemeinschaft (DFG) and the Fonds der Chemischen Industrie (FCI) for financial support. C.A.S. thanks the DFG for a Heisenberg fellowship and the FCI for a Dozentenstipendium. G.D. is the recipient of an NSERC-NATO Science Fellowship.

Supporting Information Available: Experimental details including syntheses of all compounds; Cartesian coordinates for the B3LYP/6-31G(d) optimized structures A−D, C′, and C″; CIF files for the crystal structures of **21** and **22**. This material is available free of charge via the Internet at http://pubs.acs.org.

JA061606B