CARBOSILANE DENDRIMERS:
UNIQUE MODELS FOR STUDYING THE PROPERTIES
OF NEW POLYMERIC MATTER

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Abstract

The emergence of a new type of organization of polymeric matter, namely, dendrimers has led to a change in concepts about the macromolecular world. High and strictly defined functionality, monodispersity, and the cascade principle of molecular structure formation made these systems unique objects, the interest in which has not faded to date.

Carbosilane dendrimers are of particular importance owing to the stability and inertness of their molecular backbone, high reactivity of functional groups at the silicon atom, and also the possibility of providing good analytical control over the forming structure. A wide variety of synthetic approaches to the modification of terminal groups allows for considering them as hybrid systems for the elucidation of structure–property relationships.

Based on the results of the analysis of a large number of variations of the main strategies for the synthesis of dendrimers, this review highlights the importance of studying the relationships between structure and properties using representative homologous series of new objects as a fundamental basis for exploring the dendritic form of polymeric matter.

Key words: carbosilane dendrimers, hybrid dendrimers, nanoobjects, macromolecules, polymer synthesis, amphiphilicity, crystallization, dendrimer properties, monodispersity.

Introduction

Over more than thirty years of history, the chemistry of dendrimers has emerged into a separate discipline of macromolecular chemistry, with a plethora of reviews and monographs published in the field [1–8]. The first review by Tomalia et al. [9] became the absolute record holder for the number of citations in modern chemical literature and this is an official record recognized in 2011 when D. Tomalia was included in the list of The Thomson Reuters Hall of Citation Laureates in Chemistry as one of the most cited international scientists in the field of chemistry [10].

The segregation of dendritic polymers into a separate group in a general polymer classification according to the chain structure has led to a change in concepts about the macromolecular world and the emergence of a new look at the traditional polymer chemistry [11]. While the new addition to Mendeleev's periodic table by D. Tomalia and colleagues can be regarded as a flight of fancy poorly supported by real facts, the appearance of the fourth group in the general polymer classification, which, along with dendrimers, includes hyperbranched polymers and micro- and nanogels, as well as dense molecular brushes and multi-arm stars, should be considered a fait accompli [12] (Fig. 1).

Subsequently this scheme was improved and transformed to acquire a clear form [13] (Fig. 2).

New molecular systems were united by the presence of geometric dimensions and shapes. At a certain branching degree, these structures begin to simultaneously exhibit the properties of both molecules and particles; therefore, they are

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Figure 1. Four main classes of macromolecular architectures.
called macromolecules-particles or, reflecting their sizes in the name, macromolecular nanoobjects. It is difficult to cover a great variety of works on the synthesis and investigation of dendritic objects, which are reviewed in the above-mentioned references. As this direction develops, a growing number of generalizations appear on the practical applications of new polymeric objects [14–17].

The Dendrimers book series edited by Fritz Vögtle has been summarizing the materials that cover the synthetic, supramolecular, and stereospecific chemistry of dendritic and hyperbranched molecules since 1998 [18]. Separate sections are devoted to the aspects of analysis of their structures, reactivity, and the mechanism of host–guest interactions [19], as well as the field of applied sciences, e.g., biology, medicine, materials science, etc. [20]. This series also discusses the formation of metal complexes, self-assembly, and catalysis [21].

By the first decade of the 2000s, research in the field of dendrimer chemistry had reached an unprecedented scale. A large number of reviews were published that described the synthetic strategies for dendritic growth [22–24], studies on the properties and applications of dendrimers [25–28], characterization of dendrimers using methods such as nuclear magnetic resonance (NMR) spectroscopy [29–31], mass spectrometry, matrix-assisted laser desorption/ionization (MALDI-TOF) [19], infrared (IR) spectroscopy [32, 33], etc. High but, at the same time, very specific functionality, defect-free macromolecular structure, monodispersity, and cascade growth of macromolecules attracted the attention of researchers from many fields of chemistry, physics, and biology. New molecular systems appeared to be in essence the materialized theoretical models with a nontrivial mathematical formula of the structure development.

Nowadays, the variety of specific embodiments of dendrimer systems is truly enormous. The dendrimers of various chemical nature have been synthesized and extensively explored [2, 34–42]. At the same time, the chemical technique used to construct the molecular backbone in one case or another is of great importance and often determines the level of perfection of the objects obtained by it.

All generalized examples operate with two main synthetic schemes, namely, divergent and convergent, or their combinations at different stages of growth. A combination of both schemes allows one to speak about the existence of some versatile scheme. For example, our research group described an approach that combines both divergent and convergent methods for the synthesis of organosilicon dendrimers (Fig. 3) [43]. The allylcabosilane dendrimer obtained by the divergent method, which serves as a multifunctional matrix, and the monofunctional dendron, obtained by the convergent scheme, interact with each other to form the final nonfunctional dendrimer. A large difference in the sizes of the initial compounds and the final product significantly facilitates the purification of the target dendrimer. The method proved to be effective for obtaining the dendrimers with molecular parameters that are difficult to achieve by both divergent and convergent methods.

If we talk about the fundamental aspects of the investigation of a new polymeric form, then particular attention should be drawn mainly to those synthetic approaches that ensure the synthesis of representative homologous series. Thus, poly(amidoamine) (PAMAM) dendrimers were obtained up to the 10th generation [44] using a synthetic strategy far from perfect, which utilizes large excesses (100-fold or more) of reagents. However, the low cost of the initial compounds justifies the commercial production of PAMAM dendrimers by this method.

**Different types of dendrimers**

Phosphazene dendrimers are widely represented [45–54]; however, these structures are not very stable during storage due to the propensity of the molecular backbone for secondary transformations. Nevertheless, the group of J.-P. Majoral and A.-M. Caminade [55] succeeded in producing the functional phosphorus-containing dendrimers up to the 8th generation, starting from a hexachlorocyclotriphosphazene core. The dendrimer molecules were formed by the consistent repetition of two reactions: the replacement of chlorine atoms for 4-hydroxybenzaldehyde and the condensation of aldehyde groups with H₂N–(Me)NP(S)Cl₂. At the 8th generation, this dendrimer contains 1536 terminal aldehyde functional groups.

Polyaromatic dendrimers are characterized by improved chemical and thermal stability. Moreover, they can be synthesized by the versatile approach [56], which, as was noted above, facilitates their purification. However, some peculiarities of these compounds restrict the production of high-generation
samples (Fig. 4). This is caused by the appearance of steric hindrances due to an increase in the number of rigid bulky groups in the resulting structure and a decrease in the solubility of the samples.


Nguyen et al. [57] accomplished the synthesis of rigid-chain polyphenylene dendrimers up to the 9th generation. In this case, the problem of obtaining large dendrimers was solved by using a large perylendiamine core in the repeated Diels–Alder cycloaddition. Bulky rigid-chain building blocks made available the functional groups on the surface of dendrimers, which ensured the synthesis of high-generation structures with the low content of defects. Owing to the high solubility of the resulting dendrimers, they were thoroughly purified and fully characterized. The sizes of macromolecules were determined by transmission electron microscopy (TEM). The diameters of the 8th and 9th generation dendrimers ranged from 23 nm to 33 nm, which corresponds to the values obtained by modeling linear polyphenylene chains. The authors noted an increase in the elution time of macromolecules of the higher generation dendrimers compared to polystyrene standards while studying them by gel permeation chromatography (GPC).

Among the reported families of dendrimers, carbosilane dendrimers are the most effective ones in terms of research on dendritic matter. Their synthesis can be carried out using simple and reliable strategies; therewith, both chemical operations that comprise a repeating cycle of the formation of a new layer of the molecular structure lead to the dendrimer growth. The functional groups at the silicon atom are characterized by high reactivity. At each step of chemical transformations, their conversion is strictly regulated by analytical methods, which leads to the control over the resulting structure. If necessary, the functionalized samples can be converted to their nonfunctional counterparts, suitable for almost unlimited studies, by fairly simple chemical operations. Of particular importance is the chemical inertness of the molecular backbone of carbosilane dendrimers. Under the optimal conditions, the mentioned prerequisites enable the production of defect-free structures up to high generations [13, 58, 59].

**Carbosilane dendrimers**

Let us dwell in more detail on some strategies for the synthesis of carbosilane dendrimers. The first scheme for the preparation of carbosilane dendrimers, which remains the main one to this day, was proposed in the early 1990s independently by groups of J. Roovers [60] and E. A. Rebrov and A. M. Muzafarov [61]. It consists in a multiple repetition of the elementary cycle: the Grignard reaction–the hydride addition (Fig. 5). Both reactions are well controlled, proceed with high yields, and afford the dendritic structures which are stable in the presence of the reagents used at all stages of their formation.

![Figure 5. Elementary cycle of the carbosilane bond formation.](image)

This scheme implies a change in the functionality type Si–Cl $\rightarrow$ Si–All at the first stage to provide the functional basis for the hydride addition, which results in the formation of branching points of the dendritic structure, i.e., the next layer—generation. Then the cycle is repeated. As noted above, the structure growth occurs at each stage of the interaction, which is another advantage of this strategy, given the need for multiple repetitions of the elementary cycle of the reactions to achieve certain molecular sizes. At each stage, there is a fundamental possibility to affect the character of the internal structure, density, and functionality. From this point of view, the polyallyl scheme appeared to be more preferable than the polylvinyldendrimer scheme suggested by Roover et al. [60], since it has greater potential for the production of high generation dendrimers. It is no coincidence that the polylvinyldendrimer enabled the synthesis of only four generations of the carbosilane dendrimers, while the polyallyl scheme allowed for reaching the 10th generation, and this is probably not the limit [62]. Along with functional generations, their nonfunctional counterparts were synthesized that combined both the characteristic chemical inertness of the carbosilane layer and the same inertness of the external layer (Fig. 6).

The densification of a carbosilane backbone in the polylvinyldendrimer version owing to an increase in the functionality of the external layer leads to the fact that the synthetic possibilities become

![Figure 6. General scheme for the production of polyallylcarbosilane dendrimers: functional (a) and nonfunctional derivatives (b) [62].](image)
complicated already at the low generations. Seyferth et al. [63] synthesized four generations of the carbosilane dendrimers containing 324 hydride functional groups on the periphery. The authors described the synthesis of the carbosilane dendrimer based on tetravinylsilane by alternating the reactions of hydrosilylation with trichlorosilane and organomagnesium synthesis with vinylmagnesium bromide at the growth stage. The final product was obtained after the reduction of the chlorine-substituted dendrimer with LiAlH₄. The silicon atoms in the inner sphere of these dendrimers are bound by –CH₂–CH₂– units. The 3rd generation dendrimer with the hydride groups on the periphery was obtained in 27% yield due to substantial losses at the purification step. During the preparation of the hydride–carbosilane dendrimer, difficulties arose in the synthesis of the 4th generation chlorosilyl dendrimer. According to the NMR spectroscopic data, the hydrosilylation of the vinyl-containing dendrimer of the third generation with trichlorosilane proceeded incompletely. The authors explain the incomplete conversion by low availability of the functional groups of the outer sphere due to steric hindrances. The target product was obtained under more severe synthetic conditions: performing the reaction in a sealed vial at 140 °C for 5 h. Due to the mentioned problems, this modification of the synthetic strategy with a lot of highly sensitive silyl hydride groups cannot be considered as a promising route for the production of high-generation dendrimers.

Despite all the chemical conciseness of the general scheme (hydrosilylation–the Grignard reaction), the investigations revealed also its enormous combinatorial capabilities. For example, the introduction of alkyne-functionalized reagents into the synthetic scheme at a certain step allowed for providing the dendrimer structure with the potential for future functionalization of the inner molecule sphere. Korean scientists suggested the method for introducing multiple bonds into a carbosilane dendritic backbone by the application of the cycle hydride addition–alkynylation with lithium phenylacetylide at a certain stage [64]. The choice of the reagent at the second step creates a latent functional layer in the inner sphere of the dendrimer, which greatly expands the potential for practical application of these compounds. Following the suggested methodology, the authors obtained three generations of the target dendrimers, although the 4th one was not obtained presumably due to steric hindrances. This obstacle was removed by using a bifunctional reagent, namely, dimethylchlorosilane instead of trifunctional methyldichlorosilane for the hydrosilylation of the third-generation dendrimer GF-3.

In their later work, Kim et al. [65] obtained four generations of the layered alkene–alkyne dendrimer using the technique of creating a sparse structure at the first stages of the dendrimer synthesis (Fig. 7). For this purpose, the reaction between 1,3,5-tribromobenzene and vinyltrimethylchlorosilane followed by the hydrosilylation of resulting 1,3,5-tris(dimethylvinylsilyl)benzene with trichlorosilane afforded the first generation of the carbosilane dendrimer G1P-9CI with an increased distance between the geometric center of the structure and the terminal functional groups.


Subsequent treatment of the resulting chlorosilyl derivative with lithium phenylacetylide provided the first-generation dendrimer with phenylacetylene terminal groups G1-9PA. The 2nd generation dendrimer was obtained in a similar way by repeating the cycle of chemical transformations. However, the next, third generation could not be synthesized due to the steric congestion of the external layer. To form a less spatially loaded structure, it was decided to perform the hydrosilylation of the first-generation dendrimer (G1-9PA) with the reagent with a lower functionality, namely, methylidichlorosilane, thus obtaining the 2nd generation dendrimer G2-18PA. By repeating the synthetic strategy, as was already noted, four generations of the dendrimer were obtained that bear a slightly fewer (a third less) terminal phenylacetylene groups (G4-72PA) than originally planned.

In their next work, the same research group succeeded in increasing the content of terminal phenylacetylene groups in the dendrimer [66]. For this purpose, the authors used a bulkier tetrafunctional center, namely, 1,3,5,7-tetramethyl-1,3,5,7-tetravinylcyclohexasiloxane (Fig. 8) as a branching center.

The classical cycle of reactions including the hydride addition of trichlorosilane followed by the interaction of the resulting chlorosilyl-functionalized dendrimer with allylmagnesium bromide afforded the 1st generation dendrimer bearing 12 terminal allyl groups. The subsequent formation of the alkene–alkyne structure was accomplished analogously.
to the previous report [65]. And, as this work showed, the approach proved useful [66]. The authors obtained the 4th generation dendrimer containing 96 terminal phenylacetylene groups, G4-96PA vs. G4-72PA in the previous work [67], which became an addition to the classical scheme [68].

The method proposed by Korean scientists for introducing alkene–alkyne layers into the structure of carbosilane dendrimers was used by Vodop’yanov et al. [69] to obtain a fifth-generation dendrimer with functional inner and nonfunctional outer layers. At the initial steps of the synthesis, the dendritic structure was formed by repeating the classical cycle of reactions of organomagnesium synthesis and hydrosilylation. During the production of a third-generation dendrimer, the cycle was supplemented by treatment with lithium phenylacetylide. Thus, a latent phenylacetylene functional layer was formed (Fig. 9).

The subsequent hydrosilylation afforded a 4th generation dendrimer which had two functional layers: an outer layer with chlorosilyl groups and the second, inner layer formed by substituted phenylethylene groups. Further growth of the dendrimer structure can occur both according to the classical scheme and by repeating the previous version of the cycle, depending on the goal. Obviously, the proposed hybrid synthetic strategy allows one to vary both the sizes of the carbosilane core, and thus the position of the inner functional layer, and the sizes of the resulting layers within wide limits.

The presence of the functional substituents in the inner sphere of dendrimers enables their modification with functional groups capable of complexation with metal ions. Such dendrimers hold great promise as carriers of metal complexes in the inner sphere. The first reports on the metal encapsulation into the inner sphere of dendrimers demonstrated the successful complexation of metal ions with tertiary nitrogen atoms in the inner sphere of PAMAM dendrimers [70]. Compared to the polar dendrimers such as PAMAM, carbosilane dendrimers have an inert and stable backbone but, at the same time, a large number of reactive functional groups, which suggests the possibility of forming isolated metal clusters in the inner sphere that can prevent their aggregation. This is important for the application of these systems in catalysis and production of special coatings.

An interesting way to create a latent functional layer in the architecture of a carbosilane dendrimer was presented by Tuchbreiter et al. [71]. The authors accomplished the synthesis of phenylated carbosilane dendrimers up to the 4th generation. During the following acidolysis, phenyl groups were replaced by active silyl triflate units which, in turn, can readily be substituted for anionic nucleophiles (Fig. 10). This enables the introduction of functional groups and catalytic centers into the structure of the carbosilane dendrimer both on the periphery and in the inner sphere.

The study of a new form of macromolecules requires an extensive library of homologous series of dendrimers with variable backbone nature and density, type of the terminal group functionality, etc. If we talk about the dendrimers of certain nature, it is quite obvious that the density of the resulting structure depends on the structural features of the monomer in use. We have already mentioned the successful synthesis of 10 generations of carbosilane dendrimers based on the tetraallylsilane branching center and methyldipropylensilyl groups as repeating units [61]. The use of a more highly functional monomer in the synthetic scheme—trichlorosilane instead of methyldichlorosilane—can afford very dense
structures (Fig. 11), which was demonstrated by Tatarinova et al. [72]. The mentioned work describes the synthesis of a homologous series of dense polyallylcarbosilane dendritic structures. The dendrimer of the 6th generation was obtained in 38.9% yield, had the molar mass of 221960 g/mol and 2916 terminal functional groups.


However, already during the synthesis of the 7th generation, the steric hindrances and predominance of side processes over the main ones begin to affect when trying to utilize all the terminal functionalities.

The purity of all samples after preparative chromatographic purification and their identity with the proposed structures were unambiguously confirmed by a complex of physicochemical methods (GPC, NMR spectroscopy, and elemental analysis).

The density of the inner sphere of the dendrimer is effectively controlled by varying the functionality and structure of the branching center, the functionality of the monomer, and the length of the spacer which determines the distance between branching points.

Rebrov et al. [73] suggested a synthetic scheme for the carbosilane dendritic structures that are looser than the classical ones. The authors chose the strategy of alternating di- and trifunctional monomer at the hydride addition in the cycle of reactions that form the structure of the dendrimer molecule. As a result, two series of dendrimers with double distances between the branching points were obtained. The samples of the same generation dendrimers of both series had the same number of functional groups but differed in the nature of their distribution at the chain ends: one group in the G-(n+0.5)-(C3-Si-C3)-All-1) series and two groups in the G-n-(C3-Si-C3)-All-2) series (Fig. 12).

The very first studies on the properties of the resulting compounds revealed a significant effect of the distance between branching points in the dendritic structure. Compared to the previously obtained denser classical predecessors—G-n-(C3)-All-2, they were 30% larger in size, and their glass transition points were higher by 15–20 °C.

**Hybrid derivatives based on the carbosilane synthetic scheme for dendrimers**

It is known that the nature of the terminal groups largely determines the properties of the dendrimer. During the formation of a dendritic structure, the number of terminal functionalities increases exponentially. Using appropriate synthetic transformations, the terminal groups of one type can be replaced for the groups of different nature and structure. This technique offers an opportunity to vary the properties of the initial dendrimer over a wide range. At present, a huge variety of the carbosilane dendrimers modified by the terminal groups is known.

For example, Novozhilova et al. [74] obtained the dendrimers of the 3rd and 6th generations featuring a hybrid carbosilane–ethylene oxide structure (Fig. 13).

![Figure 12. Classical synthetic scheme for the polyallylcarbosilane dendrimers with –C=C(l) distance between branching points (A) and the synthetic scheme for the polyallylcarbosilane dendrimers with double distances –C=C-Si-C=C(l) between branching points (B) [73]. (Reprinted with permission from E. A. Rebrov et al., Macromolecules, 2012, 45, 8796–8804. DOI: 10.1021/ma300957d. Copyright (2012) American Chemical Society)](image)

The modifying agents were obtained from methyl esters of the corresponding glycols through the metalation followed by the substitution of sodium ions for the allyl groups which then were utilized in the hydride addition of tetramethylsiloxane. As a result, three silyl hydride compounds differing in the length of the ethylene oxide chain were synthesized. The modified dendrimer acquired the ability to dissolve in lower alcohols, and with an increase in the number of ethylene oxide units in the substituent, loses the ability to dissolve in hydrocarbons unlike...
the original matrix.

When studying the behavior of these objects at a water–air interface, the analysis of the compression isotherms of the Langmuir monolayers showed that an increase in the rigidity of the core with the growth of the generation number leads to the formation of ordered molecular multilayers, which is typical for high-generation amphiphilic dendrimers.

The same research group synthesized hybrid dendrimers of the 3rd and 6th generations with 2-phenylethyl groups on the periphery [75]. Owing to the related nature of the terminal groups, the samples showed good compatibility with the polystyrene matrix which was used to obtain the composite materials. The modified dendrimer was studied as a nanosized core–shell filler [13]. During the experiment, the effect of the dendrimer size and the ratio of the components on the thermodynamic characteristics of the composite was evaluated. A significant impact of the generation number of the dendrimer filler and its concentration on the glass transition point of the composite was established.

A good example of the effect of the type of terminal groups on the dendrimer properties was presented by Tereshchenko et al. [76]. The authors obtained three derivatives of the 5th generation carbosilane dendrimer with different terminal groups: diundecylsilyl, diundecylsiloxane, and tetrasiloxane (Fig. 14).


The samples were obtained by the hydride addition of the corresponding modifying agent at the terminal groups of the allyl-functionalized dendrimer matrix in the presence of a Pt(0) catalyst. The high-precision adiabatic calorimetry was used to determine their thermodynamic characteristics. The results obtained showed that the glass transition points of the samples vary greatly depending on the nature and structure of the terminal groups. Thus, dendrimer VI with flexible siloxane terminal groups, which are characterized by weak intermolecular interactions, has \( T_g = 163 \) K, while for dendrimer IV with the rigid undecyl substituents \( T_g = 209 \) K. Dendrimer V bearing the same rigid moieties in the structure of the terminal groups but bound to the carbosilane core through a flexible siloxane bond, shows the intermediate value of \( T_g \) equal to 190 K.

Minyaylo et al. [77] presented the synthesis of new organoelement dendrimers based on polyallylcarbosilane dendrimers of the 1st, 3rd, and 5th generations and a mercapto derivative of a polyhedral carborane (Fig. 15).


The target compounds were synthesized by the radically initiated hydrothiolation. This method belongs to the so-called click reactions which have been widely used for the synthesis of dendrimers [78]. This type of reactions should be stereospecific, thermodynamically very favorable (a single product is formed), proceed with high yield, and have a wide range of applications. These requirements are met by a number of reactions, among which the azide–alkyne cycloaddition [79, 80], the Diels–Alder reaction [81, 82], as well as thiol–ene and thiol–yne addition reactions [83–85] are most frequently used for the synthesis of dendrimers and their modification.

Unlike the liquid initial dendrimer, the compounds obtained by Minyaylo et al. [77] are white finely dispersed powders and combine the flexibility of a carbosilane core and the rigidity of a shell formed by polyhedral carborane units. These systems are stable and thus can be used as model compounds for studying the structure–property relationships, similarly to the carbosilane dendrimers featuring different terminal groups [76, 86, 87]. On the other hand, the possibility of activation of the C–H bond in the carborane polyhedron, which the authors mention, opens up prospects for further modification of the terminal groups and the production of new hybrid systems. The structures and purity of the resulting compounds were confirmed by a complex of physicochemical methods.

Zhang et al. [88] used a combination of thiol–ene addition click reactions under different conditions: the thiol–ene Michael additions catalyzed by an organic base and the radical-mediated thiol–ene reactions initiated by a photoinitiator. The carbosilane dendrimers were constructed on the basis of a monomer bearing electron-deficient carbon–carbon double bonds as well as nonconjugated carbon–carbon double bonds. The siloxane units were introduced as decoupling points between these two types of carbon–carbon double bonds. The sequential repetition of the thiol–ene click reactions under different conditions afforded a fifth-generation dendrimer with 54 peripheral functional groups in high yield. Another advantage of this synthetic strategy is its rapidness. The synthesis and isolation of the target product can be accomplished in one day (Fig. 16).
A very effective method for the synthesis of hybrid dendrimers is block assembly, when the target dendrimer is obtained on the basis of preliminary synthesized structural blocks with the corresponding functional groups: a traditional multifunctional dendrimer and a monofunctional monodendron obtained by a convergent scheme. The monodendron is used in excess to ensure the complete conversion of the active groups in a multifunctional dendrimer. This scheme affords the dendrimers of higher generations in a single step. Therewith, an increase in the molecule sizes occurs much faster than during the layer-by-layer structure formation by the divergent method. Another important advantage of the block assembly is significant simplification of the purification of the target product owing to a large difference in the molar masses of the reaction mixture components.

Tarasenkov et al. [90] reported the block assembly of the hybrid carbosilane–thioether dendrimers. For this purpose, the monodendrons of the 1st and 2nd generations bearing a thiol functional group at the focal point were synthesized. Their subsequent interaction with the 3rd generation polyallylcarbosilane dendrimer under conditions of the photoinitiated thiol–ene addition yielded the target 4th and 5th generation dendrimers with shielded sulfur atoms in the structure. These compounds can be used to bind with metal ions and to form isolated metal nanoclusters. All the thio decyl dendrimers are amorphous–crystalline, as indicated by the presence of an endothermic peak on the DSC curves, whereas the dendrimers containing bidecylsilyl groups on the periphery lose their propensity for ordering due to a decrease in the mobility of the terminal units, and thereby are amorphous (Fig. 18).
To verify the possibility of modifying a higher generation dendrimer and obtaining the samples with a high content of sulfur atoms in a dendritic molecule, the authors accomplished the interaction between the 6th generation allyl-functionalized dendrimer and decanethiol under similar conditions to obtain G6-256S-Dec. The reaction was complicated by side condensation processes. According to the results of GPC analysis, a higher molecular weight fraction was present in the crude product.

Serkova et al. [91] synthesized the hybrid carbosilane–polyphenylene dendrimers that consist of a flexible carbosilane inner part and a rigid polyaromatic shell (Fig. 19).

![Figure 19. Synthesis of the hybrid dendrimers with the carbosilane core and polyphenylene dendrons in the external shell [91]. (Reprinted with permission from E. S. Serkova et al., Polymer, 2018, 138, 83–91. DOI: 10.1016/j.polymer.2018.01.047. Copyright (2018) Elsevier)](image1)

The investigation of the thermodynamic properties of the resulting compounds by differential scanning calorimetry (DSC) revealed an increase in the glass transition point of the first-generation dendrimer G1Si13Ar32 by 150 °C relative to the polyallylcarbosilane dendrimer, the glass transition point of which is −101.15 °C [92]. An increase in the number of rigid aromatic groups in the shell of the G1Si13Ar64 molecule increases the glass transition point by another 100 °C. However, an increase in the size of the carbosilane core at the same number of phenylene terminal groups in G2Si29Ar64 does not affect its value, thereby confirming the determining role of the terminal groups on the dendrimer properties, in particular, the glass transition point [13].

The results of investigations by wide-angle X-ray scattering (WAXS) indicated weak ordering in the case of G1Si13Ar32 and G2Si29Ar64. As the density of the shell (G1Si13Ar64) increases, the reflections on the WAXS curve almost completely disappear, which indicates the suppression of ordering processes.

In the same work, the dendrimers based on a rigid nonpolar hydrophobic aromatic core and a flexible, mobile, nonpolar and hydrophobic carbosilane shell were synthesized using the reverse order of block assembly (Fig. 20).

![Figure 20. Synthesis of the hybrid dendrimer with the polyphenylene core and the carbosilane shell [91]. (Reprinted with permission from E. S. Serkova et al., Polymer, 2018, 138, 83–91. DOI: 10.1016/j.polymer.2018.01.047. Copyright (2018) Elsevier)](image2)

Fluorine-containing carbosilane dendrimers

Other striking examples of the hybrid carbosilane dendrimers are amphiphilic polyfluorinated carbosilane dendrimers. The C–F bond has high energy and is somewhat longer than the C–H bond, which determines the high chemical and thermal stability of polyfluorine-containing compounds. They display low polarity, weak intermolecular interactions, hydro- and oleophobicity. Due to the mentioned features, polyfluorocarbons exhibit biological inertness and are attractive research objects in the field of biomedicine. Perfluorocarbons are used in medicine as F-contrasting agents in magnetic resonance imaging (MRI) [94]. Owing to the high oxygen solubility in them, perfluorocarbons are used as blood substitutes [95] and can serve as means of safe oxygen delivery to tumors [96, 97], thereby improving the effectiveness of radiotherapy.

A combination of the regular and highly functional structure of carbosilane dendrimers and the advantages provided by the involvement of fluorine-substituted moieties holds great promise for the discovery of interesting properties of these compounds.

The fluorine-containing dendrimers were obtained in high yields by the hydrosilylation of a hydride-terminated carbosilane dendrimer with allyl-1,1-dihydrophedecylfluorononyl ether [98] (Fig. 21). However, the authors noted the incomplete conversion of the Si–H groups, which is obvious from the 29Si NMR spectrum of the fluorinated product.


Casado et al. [99] used the hydrosilylation of the second-generation allyl-functionalized carbosilane dendrimers with silanes HSiMe2[(CH2)nR] (1a: n = 2, R = n-C6F15; 1b: n = 3, R = C6F13) to obtain modified samples with the very low intrinsic viscosity. The calculated hydrodynamic radii for samples [G-1],
A number of carbosilane dendrimers up to the 3rd generation functionalized with perfluoroalkyl terminal groups were reported [100]. The 3rd generation dendrimer contained 108 terminal groups in the external layer. The quantitative surface perfluoroalkylation was carried out by the free radical addition of 3,3,4,4,5,6,6,7,7,8,8,9,9-tridecafluoro-octylmagnesocene. The purity and structures of the resulting compounds were confirmed by the results of GPC and $^1$H NMR spectroscopic analysis. The yield of the third-generation dendrimer was 65%.

The dendrimers obtained were studied by WAXS. It was noted that the zero generation dendrimer was obtained in the form of crystals, whereas G-1 (12 terminal groups) showed the formation of a highly ordered smectic mesophase at the temperatures from −15 to −30 °C. In contrast, G-2 (36 terminal groups) and G-3 (108 terminal groups) did not form mesophases; however, a transition to a hexagonally ordered array of columns was likely to be observed. The generation number-dependent thermal behavior was attributed to the denser packing of perfluorohexyl groups on the dendrimer surface. A transition to high generations led to a loss of the solubility in conventional nonpolar aliphatic solvents, while maintaining the solubility in fluorinated solvents. A decrease in the solubility is probably associated with an increase in the shielding degree of the carbosilane core by bulky perfluoroalkyl groups with an increase in the generation number.

Polyfluorinated amphiphiles find extensive use in various fields, for example, they can be used as delivery vehicles for gene material and secondary surfactants in drug delivery [101, 102]. Polyfluorinated carbosilane dendrimers with hydroxy groups on the periphery represent a new class of compounds that may have unique surfactant properties. These amphiphilic dendrimers can be used as phase transfer agents in synthesis and catalysis [103]. Omotowa and Shreeve [104] reported the synthesis of this type of carbosilane dendrimers, which had both long perfluorinated substituents and hydroxy groups at the branch termini (Fig. 22).

In a number of reports on the preparation of fluorine-containing carbosilane dendrimers [105, 106], the synthesis of hybrid carbosilane dendrimers with variable density of the fluorinated layer is presented. The works deal with the synthesis of the 7,5 generation dendrimers with a completely substituted tris-$\gamma$-trifluoropropylsiloxane layer as well as the dendrimer having in the outer layer, along with tris-$\gamma$-trifluoropropylsiloxane groups, cyclic siloxane moieties. The purity and structures of the resulting compounds were confirmed by the results of GPC, NMR and IR spectroscopic analysis, as well as elemental analysis. It was concluded that the perfluorocarbon carbosilane-siloxane dendrimers have a denser external layer than their polybutylcarbosilane counterparts. The introduction of crosslinks between the branches makes them even more rigid objects which do not respond to the solvent quality. Further investigations of this group showed that the introduction of perfluorinated moieties into the shell of the carbosilane dendrimers provides control over the solubility of these dendrimers of both low and high generations [107]. The nonmesogenic fluorine-containing substituents increase the solubility of the resulting systems at high generations, which enables a complex study of their hydrodynamic properties in comparison with irregular analogs (Fig. 23).

**Figure 22.** Perfluorinated hydroxy-functionalized carbosilane dendrimer [104]. (Reprinted with permission from B. A. Omotowa, J. M. Shreeve, Macromolecules, 2003, 36, 8336–8345. DOI: 10.1021/MA034326E. Copyright (2003) American Chemical Society)


### Hydroxy-containing carbosilane dendrimers

The lipophilicity of carbosilane dendrimers restricts the potential of their use and the possibility of in-depth investigations of their structures and properties. Therefore, conferring them polar qualities as well as developing the methods for controlling the lipophilic–hydrophilic balance of the molecule is a very popular task. The reports on the preparation of hydroxy-functionalized carbosilane dendrimers [108] appeared soon after the first work on the synthesis of their hydrophobic precursors.

Lorenz et al. [108] obtained the carbosilane dendritic polyols by exhaustive hydroboration–oxidation of an allyl-
The carbosilane polyhydroxy dendrimers are promising for use as molecular containers for drugs due to the large number of hydroxy groups in the external layer of the dendrimer [115].

**Ionic carbosilane dendrimers**

The development of means for targeted delivery of genes and drugs into the cell of a living organism is a very popular research topic in the field of biomedicine. Nonviral delivery vehicles based on the complexes of nucleic acids with liposomes (lipoplexes) or dendrimers (dendriplexes) [116] are not so effective but safer than the viral ones. Cationic dendrimers form dendriplexes by interacting with negatively charged nucleic acids. These formations are able to penetrate the cell membrane, and the state of the complex stabilizes nucleic acid molecules, protecting them from destruction under physiological conditions.

Owing to their stability, biocompatibility, nontoxicity, and ample opportunities of functionalization, carbosilane dendrimers are promising research objects in this area. However, with all the undeniable advantages for use in biomedicine, it is necessary to convert them into a water-soluble form.

The cationic carbosilane dendrimers with peripheral substituents NMe3, PMe3, P(Et2)(CH2)3OH, PBu3, P(C6H4)2OME3, and Ph3P were synthesized and thoroughly characterized. Their structures were evaluated by computer simulation methods [117]. The dendrimers containing butyl, methoxyphenyl, and phenyl substituents with an iodide anion as the counterion showed only low solubility in water. The replacement of iodide anions for the chloride ones led to a significant increase in the water solubility, up to >100 mg/mL, which enabled the following investigation of their cytotoxicity.

The dendriplexes based on dendrimers with P(C6H4-OMe)3 and Ph3P substituents showed very low cytotoxicity and preferential accumulation in mitochondria, where appropriate drug delivery could be targeted.

The carbosilane dendrimers with anionic carboxylate G6X(C6H4CO2Na)m and sulfonate G6X(C6H4SO3Na)m groups on the periphery, synthesized up to the third generation based on two different centers 1,3,5-(HO)3C6H4 and Si(C6H4)3, were reported [118]. The anionic groups on the periphery made these dendrimers soluble in water, despite the hydrophobicity of the carbosilane backbone. The behavior of these diphilic dendrimers in an aqueous medium was studied, taking into account the differences in internal and external structures, as well as the differences between the two types of anionic groups. The carboxylate-containing dendrimers were obtained by two methods, namely, by the hydrolysis of hydride-functionalized polyallylcarbosilane dendrimers with unsaturated β-alanine N-(3-methoxy-3-oxopropyl)-N-2-propen-1-yl-methyl ester ((C6H3)N(C6H4CO2Me)2) and by the reaction of amino-functionalized carbosilane dendrimers G5Si(NH3)2m with methacrylate under the Michael addition conditions. The first method was preferred because it allows for avoiding the laborious step of isolating the amine-containing dendrimers. The total negative charge of the resulting dendrimers in water was measured by pH titration. The investigations performed revealed
different behavior of the carboxylate and sulfonate dendrimers, associated with the different inductive effects of the presented anionic groups as well as their different acid-base properties.

Already at the early stage of the development of dendrimer chemistry in 1991, G. Newkome, one of the pioneers in this area of polymer chemistry [119], noted that amphiphilic dendrimers in the charged and neutral states are in essence molecular micelles. The peculiarities of the micellar nature of dendrimers were described in the review by Percec et al. [120], which presented the synthetic aspects of Janus dendrimers and glycodendrimers capable of self-organization in an aqueous medium. These structures are self-assembling amphiphiles capable of forming monodisperse, stable and multifunctional single-layer and multilamellar vesicles of the onion type and other complex architectures. The sequential block synthesis provides structure control at the molecular level, which ensures the achievement of topologies with the given structure and density. The synthesis of amphiphilic Janus dendrimers containing linear and branched alkyl chains in the hydrophobic part was described by Buzacchera et al. [121]. Thirteen dendrimers of amphiphilic nature were obtained by the stepwise modular synthesis from natural phenolic acids and fully characterized. These systems are actively explored as nucleic acid delivery agents in the field of genetic medicine [122].

Carbosilane systems did not remain afloat from this important direction. A similar approach based on subtle understanding of the differences in the reactivity of unsaturated groups in the limonene molecule was demonstrated by Ryzhkov et al. [123]. The great combinatorial opportunities of the new platform are likely to promote the development of this direction based on carbosilane systems in the nearest future.

Hence, we have considered a significant number of variations of the major synthetic strategies and can conclude that the main scheme for the synthesis of carbosilane dendrimers with parallel synthesis of nonfunctional counterparts is of great fundamental importance [59]. Just this material was used to perform a huge array of studies, which made it possible not only to determine the dependence of the intrinsic viscosity and density on the number of generations for representative homologous series of dendrimers, but also to conduct a comprehensive study of other physical properties that require the use of complex scientific equipment. Even the measurement of the density of dendrimers of different homologous series, differing in the structure of the molecular framework, led to deeper understanding of the accumulated material published by that time [72]. It became clear, for example, that the postulated extreme dependence of the number on the generation number is not of general nature. In this particular case, it did not depend on the generation number [66]; for denser systems with a tetrafunctional branching center and a tetrafunctional monomer, the density increased with the generation number. A similar character of the dependence was observed for siloxane systems with a very short spacer [124]. These data served as a kind of benchmark for studies on modeling the behavior of dendrimers in block [125–128]. The investigations by small-angle neutron scattering allowed for defining the sizes of dendrimers in solution and estimating the solvent volume in its inner sphere [129]. The result of investigations on the thermal characteristics of the dendrimers was the discovery of a second transition in the dependence of heat capacity on temperature in high-generation samples [130], which was reproduced on all the systems of carbosilane dendrimers explored, with slight changes depending on the density of the molecular structure [131–134]. This transition, which was not understood for a long time, played an important role in the studies since it coincided with a change in the aggregate state of the dendrimer samples as the number of generations increased. A phenomenological explanation based on the assumption of the formation of a specific entanglement network of dendrimer branches as the solvent is removed remained the only one for a long time [135]. Only recently it was confirmed by the discovery of the crystallization phenomenon of high-generation dendrimers [136]. It was shown that the formation of an amorphous mass with a pronounced yield point occurs first. However, under the conditions of sample annealing in solvent vapors, the clamped branches are released and the final ordering takes place. The dendrimer forms a crystal lattice (Fig. 24).

![Figure 24. SANS curves for G-5 (a), G-6 (b), G-7 (c), and G-8 (d) at different temperatures [136]. (Adapted with permission from A. V. Bakirov et al., Soft Matter, 2018, 14, 9755–9759. DOI: 10.1039/C8SM02145G. Copyright (2018) Royal Society of Chemistry)](image)

These studies finally confirmed the objectivity of the concept of high-generation dendrimers. It is this state of dendrimers that can be considered as a new type of polymeric matter. Most researchers confine their investigations to low-generation dendrimers, not taking into account the fact that a qualitative transition in properties occurs just at high generations.

State-of-the-art and future outlook

To date the interest in dendrimer systems has not faded out. However, most of the examples considered above show that, in the initial period, the main focus was on the development and comparison of different synthetic schemes, whereas in a later period, the research efforts concentrated on various applied aspects of the dendrimer chemistry. This, in turn, led to the fact that most of the works deal with the low-generation systems, showing the possibility of their application in different fields, where medicine [137] and catalysis [138] are especially popular.

Some areas of practical application, such as, for example, photonics and microelectronics, demonstrate the successful use of low-generation dendrimers. Ponomarenko et al. [139] reported the synthesis of the first-generation bithiophenesilane dendrimer with the possibility of obtaining light-emitting diodes.
on its basis. A number of quatrothiophene-containing carbosilane dendrimers were also synthesized by the same research group [140]. The resulting dendritic structures consist of a highly branched dendritic core with flexible aliphatic spacers bearing oligothiophene units as terminal groups, which determine the semiconductor properties of the molecule. The branched core increases the local density of terminal oligothiophene groups, thus facilitating their self-organization. The authors note that the low-generation dendrimers are the most successful structures, suggesting that a further increase in the volume of the dendritic core leads to a decrease in the effective mobility of the terminal groups and, as a result, to a decrease in the ability to order. This observation is consistent with a decrease in the crystallinity degree in these systems, as evidenced by the DSC data.

Borshehev et al. [141] reviewed the nanostructured organosilicon phosphors and discussed the successful use of dendritic organosilicon molecular antennas to increase the efficiency of organic phosphors.

In the field of fundamental research of low-generation monofunctional dendrimers, of note are the above-mentioned works [120, 121] in which the behavioral peculiarities of diphilic monodendrons are consistently studied, generalized, and collected into a huge library that allows one to regulate the processes of their self-organization. The use of knowledge accumulated in the field of biology enables the simulation of the properties of living matter. The bactericidal vesicles capable of isolating bacteria were created on the basis of diphilic dendrimers [142–144].

As for the consistent fundamental approach to the investigation of a new form of polymeric matter, developed by the Russian academic school, it is certainly bearing fruit in understanding the properties of dendrimers as a special type of polymers with a pronounced dualism of properties in macromolecule-particle coordinates. Like classical polymers, they consist of many repeating units, display the propensity to swell and collapse depending on the quality of the solvent [129, 145], and their glass transition temperature increases with increasing molecular weight, which tends to a certain limit. However, unlike classical polymers, in solutions they behave like solid spheres impermeable to the solvent [62, 73, 77].

During the targeted investigation of a new type of polymeric matter [109], unique multicenter polylithium initiators [146] were created that have no analogs in polymer chemistry. They were used as the basis to create multiarm polymer and copolymer [147] stars as well as dense molecular globules with a unique set of properties [148, 149]. The concept of inner and outer spheres was defined [150].

Finally, a systematic study of carbosilane dendrimers led to the achievement of their highly ordered state [136] and the discovery of the possibility of their use as a new type of polymeric material with a unique set of properties [135] for the production of membranes [151, 152] and molecular fillers [153, 154].

Hence, using the example of carbosilane dendrimers, the effectiveness of the fundamental approach to the creation of new polymeric forms was once again confirmed, since after the completion of this stage of solving the problem of structure–property relationships, the researchers involved in the dendrimer chemistry will encounter with new broad prospects associated with the uniqueness of their properties and the enormous combinatorial possibilities of their regulation.

Conclusions

Forty years have passed since the discovery of dendrimers. Have our ideas about this new form of polymeric matter changed? Certainly, they have changed, they have become wider, deeper, and more reasonable. We know that dendrimers are polymers, which was not obvious at the initial stages of their development. Dendrimers are characterized by a dualism of properties in the macromolecule-particle coordinates, with the predominance of the molecular properties [155]. We know that this is the most regular and controllable form of polymeric matter, and the fullness and uniqueness of their properties are manifested in high-generation dendrimers. This is the most mathematized form of polymeric matter, a materialized theoretical model, which, by its appearance, gave a powerful impetus to the refinement of many theoretical foundations of polymer science and computer modeling as well. We have an idea of a huge number of variations of two basic schemes: divergent and convergent. This is a foundation for extensive research on the use of dendrimers in the field of medicine and catalysis, photonics and molecular electronics, molecular composites and supersurfactants.

The solution of what specific tasks is most relevant for the successful development of this area? First of all, this is the further improvement of synthetic schemes for obtaining dendrimers with the given structure and predetermined useful functions. The implementation of green chemistry principles into the processes of their production, consistent design of new dendrimer systems for specific practical applications. The development of block assembly (construction) principles for homodendrimers and block-co-dendrimers. The expansion of areas of effective practical application of dendrimers.

A powerful impetus to the development of the entire field of dendrimer chemistry is given by the unique results of studying the phenomenon of ordering of high-generation dendrimers. The peculiarities of their packing determine a transition from a metastable amorphous to crystalline form of ordering. During crystallization, they form excellent plastic crystals with a packing density higher than that of solid spherical bodies. From this moment, a new life of dendrimers begins: as a highly ordered material, the structural parameters of which can be controlled at the molecular level.

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