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Probing the versatility of shape-persistent tetraphenylmethane dendrimers by modification of the skeleton.

Julio I. Urzúa,^{a,†} Sandra Campana,^a Massimo Lazzari^b and Mercedes Torneiro^{a*}

^aDepartamento de Química Orgánica, Facultade de Química, Universidade de Santiago de Compostela, 15782, Santiago de Compostela, Spain.

^bCentro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS) and Departamento de Química Física, Universidade de Santiago de Compostela, 15782, Santiago de Compostela, Spain.

* E-mail: mercedes.torneiro@usc.es

† Present address: Comisión Chilena de Energía Nuclear, calle Nueva Bilbao 12501, Comuna de los Condes, 7600713, Santiago de Chile, Chile.

ABSTRACT. Tetraphenylmethane has emerged as a recurrent building block for advanced porous materials such as COFs, PAFs and hypercrosslinked polymers. Guided by a similar design principle, we have previously synthesized shape-persistent dendrimers with tetraphenylmethane nodes and ethynylene linkers. Here we report the generality of our approach by describing new dendritic architectures built from tetraphenylmethane. First, we prepared expanded dendrimers where the tetrahedral units are bonded through larger rigid rod spacers. Among the different synthetic strategies tested, the convergent route, with alternating steps of Pd-catalyzed Sonogashira coupling and alkyne activation by removal of TMS masking groups, efficiently afforded the first- and second-generation dendrimers. A second type of compounds having a linear diyne at the core is also described. The dendrimers of generations 1-2 were also synthesized by a convergent approach, with the diyne being assembled in the last step of the synthesis by a Glaser oxidative homocoupling of the corresponding dendrons bearing a terminal alkyne at the focal point. A third-generation dendrimer was also successfully prepared by a double-phase strategy.

Introduction

The tetrahedral tetravalent structure of sp^3 carbon is responsible, in conjunction with the diversity of functional groups and the stability of the C-C bond, of the structural and functional variety of organic compounds. Tetraphenylmethane can be considered as an expanded sp^3 carbon that reproduces the same tetrahedral geometry in a larger structure when radially substituted, i.e. at the *para* positions of the aromatic rings. In fact, tetraphenylmethane is a rigid three-dimensional building block widely used to assemble the structural framework of artificial systems of considerable size. To name just a few, it has been employed to build tetrahedral structures,¹ in self-assembled and supramolecular systems,² as building block for light-emitting and antennae materials,³ in electronically active materials,⁴ in liquid crystals,⁵ for rotaxane stoppers⁶ and as core of shape-persistent dendrimers.⁷ A field of recent development where tetraphenylmethane has been extensively employed is that of organic porous materials. In particular, it has been used as building block for molecular cages,⁸ reticular materials (MOFs and COFs)⁹ and amorphous porous frameworks (microporous polymers, PAFs and related materials).¹⁰ In this last case,

the tetraphenylmethane units are hypercrosslinked either directly or through linear spacers to create diamond-related amorphous frameworks with internal voids or pores resulting from the radial stiffness and inefficient packing of the building blocks.

We have recently reported the synthesis and fluorescent properties of shape-persistent dendrimers with tetraphenylmethane nodes and ethynylene linkers of generations 1 and 2 (e.g. **G1a**, Fig. 1).¹¹ The interest of these macromolecules lies in their privileged architectures, with a protein-like globular structure from the second generation. They have a hydrophobic interior with well-defined cavities and the polar terminal groups are effectively located at the periphery with reduced possibilities of backfolding. Being the soluble and structurally-regular analogs of microporous polymers, dendrimers of this type can be potentially used for separation technologies, for gas storage, in catalysis, sensing, and to build multichromophoric luminescent materials or nanomachines.

In this paper, we investigate the scope of the convergent, divergent and double-phase synthetic methodologies to access new members of this family of macromolecules. In addition, we show the versatility of this modular design by preparing dendrimers with modifications at their skeleton, either at the branches or the core. In the first case, our goal is the synthesis of molecules with an expanded structure, which can be accomplished by introducing larger rigid rod linkers between the tetraphenylmethane nodes. As an example, we selected for this work dendrimers **G1b** and **G2b** (Fig. 1), which have ethynylene-phenylene-ethynylene spacers. As a consequence, they have bigger size and molecular weight than the parent compounds (**G1a** and the analog second-generation dendrimer), while maintaining the shape-persistent structure. Three-dimensional models show that **G1b** has a star-like shape, whereas **G2b** has a globular structure with well-defined inner cavities of bigger volume than the parent compound. On the other side, we also describe in this work dendrimers **G1c**, **G2c** and **G3c** (Fig. 1), with a diyne core. The overall structure is more similar to the related tetraphenylmethane-cored prototypes (e.g. **G1a**), but with an ovoid instead of spherical globular shape resulting from the linear symmetry of the core.

Figure 1. Structure of dendrimers of the **a** (G1a), **b** (G1b, G2b) and **c** series (G1c, G2c, G3c).

Results and Discussion

We started our work with the synthesis of the **b** series macromolecules. We envisaged that the expanded dendrimers could be easily accessed by a convergent route based on Sonogashira Pd-catalyzed couplings, previously demonstrated in our group for the prototype tetraphenylmethane dendrimers with ethynylene linkers.^{11a} The first generation dendron or terminal unit (**4**, Scheme 1) was prepared by coupling of the alkyne **1**¹¹ with the aryl bromide **2**¹² using Pd(PPh₃)₄ as catalyst in the presence of PPh₃, CuI and 4 Å molecular sieve in piperidine at 100 °C, followed by removal of the TMS group at the focal point by

treatment with sodium hydroxide in methanol. A new Sonogashira coupling of the dendron **4** with the core tetraiodide **5**,^{11,13} using the standard preceding conditions, afforded the first-generation dendrimer **G1b** in excellent 83% yield for the three steps.

Scheme 1. Convergent route to dendrimers G1b and G2b.

To address the synthesis of the second-generation dendrimer, we first prepared the branching unit **7** by coupling of the acetylene **6**¹⁴ and the tetraiodide **5** using $\text{Pd(PPh}_3)_4$, PPh_3 , CuI and piperidine in THF at rt. The low yield in this reaction (30%) is caused by the statistical reaction of the spacer with the aryl iodides of the tetravalent core. To avoid the formation of undesirable amounts of by-products resulting from coupling of multiple acetylenes to the core, an excess of the core building block **5** was used, which can be easily separated as the insoluble material in the reaction crude. The Pd-catalyzed coupling of the branching and the terminal units, **7** and **4**, respectively, under standard conditions gave, in good yield, the protected second generation dendron, **8**. Desilylation with NaOH and Sonogashira coupling with the core

unit **5** afforded in good yield the second-generation dendrimer **G2b**. **G1b** and **G2b** were fully characterized by MALDI-TOF mass spectrometry and $^1\text{H}/^{13}\text{C}$ NMR spectroscopy and they showed a clean SEC trace with a single peak with retention times according to their molecular weights. A common property of this series of expanded dendrimers is their low solubility, that is useful for their isolation, as they precipitate in the reaction media as white solids. They are very stable, remaining unchanged after several days exposed to air on the bench. In addition, they show a characteristic luminescence that can be observed as a purple glow by illuminating a dilute solution under an UV lamp or as a bright blue spot upon UV irradiation of a sample on a TLC plate. They show a good stability,

Scheme 2. Divergent and double-phase strategies for the b series of dendrimers.

At this point, we decided to apply our recently developed triazene-based divergent route^{11b} to this series of dendrimers for comparative purposes. Therefore, we explored the divergent approach to **G2b** using as starting tetraphenylmethane building blocks the *tris*(triazene) derivatives **10**^{11b} and **11**^{11b} that were coupled to either spacer **2** or **6**, respectively (Scheme 2). In both cases the desired protected expanded dendron **12** was obtained with good to moderate yields. Subsequent desilylation and coupling to tetraiodide **5** afforded the triazene-terminated first generation dendrimer **G1b-N₃** in 63% yield for the two steps, which was transformed in the iodo-terminated dendrimer **G1b-I** by treatment with MeI at 120 °C (95% yield).

Unfortunately, our efforts to grow this dendrimer by coupling with dendron **4** were unsuccessful, yielding complex mixtures, in which compound **G2b** could not be detected. The reaction of **G1b-I** with dendron **9** was also tested in an attempt to prepare the corresponding third-generation dendrimer (**G3b**, structure not shown) by a double-stage method, but the desired dendrimer could not be detected in the resulting complex reaction mixtures.

Next, we turned our attention to the synthesis and characterization of the diyne-cored dendrimers of the **c** series. In addition to their interesting structure, these compounds should be easily accessible by Glaser oxidative homocoupling¹⁵ of the corresponding dendrons bearing a terminal alkyne at the focal point. Of the many conditions reported in the literature for this reaction, we selected those that were favorable to the dissolution of the substrates. We started by testing the reaction of **1** with different copper salts as catalyst in CH₂Cl₂,¹⁶ but neither CuI or CuCl in combination with diethylamine, piperidine or pyrrolidine as bases and in the presence of oxygen gave the desired product **G1c**, and the starting material was recovered unaltered. Similar negative results were obtained when the reaction was carried out with Hua's conditions¹⁷ – CuCl and piperidine in toluene.

Scheme 3. Convergent route to dendrimers **G1c** and **G2c**.

Our observation during the synthesis of the tetraphenylmethane-cored dendrimers (e.g. **G1a**) that small amounts of the diyne-cored dendrimers were sometimes obtained as by-products, led us to essay the Sonogashira conditions under air at rt. So, the reaction of **1** with Pd(PPh₃)₄ (0.1 eq.), CuI (0.1 eq.) and piperidine (13 eq.) in THF in the presence of air afforded the desired dendrimer **G1c** in low yield, which was improved to 98% yield by increasing the amount of CuI to 2 eq. (Scheme 3). To undertake the synthesis of the dendrimer **G2c**, we first developed a new synthetic route to the protected second-generation dendron **17**. Instead of coupling the spacer to the tetraiodide **5** with ~30% yield, as in the previously reported method,^{11a} and in the strategy followed to prepare **8** (Scheme 1), we reacted the terminal unit **1** to the known triiodide **14**⁶ to obtain the phenol **15** in 73% yield (Scheme 3). Treatment with triflic anhydride gave the intermediate triflate **16**, which was coupled with the TMSA spacer to yield the desired protected dendron **17** (90% for the two steps). Desilylation to give the dendron **18**^{11a} followed by Glaser homocoupling in the above optimized conditions afforded the final second-generation dendrimer **G2c** in excellent 96% yield (two steps).

Once demonstrated the feasibility of the convergent method to access the **c** series of dendrimers, we considered worth to attempt the double-stage strategy for the synthesis of a dendrimer of third generation. The Glaser homocoupling of the *tris*(triazene) **10** gave the triazene terminated dendrimer **G1c-N₃** in excellent yield (Scheme 4). Treatment with methyl iodide afforded the hexaiodide **G1c-I** that worked as a supercore for dendrimer growth by Sonogashira reaction with dendron **18**. In this case, the double-stage coupling proceeded smoothly to give the dendrimer **G3c** in 66% yield for the last two steps.

Scheme 4. Double-phase synthesis of G3c.

Dendrimers **G1c**, **G2c** and **G3c** were conveniently characterized (^1H and ^{13}C NMR, MALDI-TOF MS) and showed a clean SEC trace with retention times according to their sizes. They are stable white solids compounds with good solubility in common solvents (THF, CH_2Cl_2 , CHCl_3). By visual inspection they do not show luminiscent properties as in the case of the previous series.

In conclusion, we have shown that tetraphenylmethane-based shape persistent dendrimers have very versatile modular structures that are accessible by different synthetic methodologies. In this work we have prepared two new series of compounds with unique geometrical characteristics, either with a expanded structure or with a diyne core. Both families were easily prepared by a convergent strategy. Whereas the convergent and double-phase routes were unsuccessful for the synthesis of **G2b** and **G3b**, respectively, **G3b** was efficiently prepared by a double-stage methodology. The chemistry involved in those syntheses is basically an iterative process based on Pd-catalyzed Sonogashira couplings of terminal alkynes with aryl iodides and triflates, with alternating steps of activation of masked groups. In the case of the **c** series there is also a key step consisting of a Glaser homodimerization to assemble the core diyne. This is the first example of a double-stage strategy for rigid tetraphenylmethane dendrimers, and also we report the first dendrimer of third generation of this class. Further studies are being carried out in our laboratories to evaluate the properties (e.g. porosity, fluorescence) of these new macromolecular materials, which will be reported in future papers.

Experimental Section¹⁸

Protected dendron 3. A Schlenk tube equipped with a stirring bar was charged with **1**¹¹ (200 mg, 0.46 mmol), **2**¹² (175 mg, 0.69 mmol), CuI (4 mg, 0.023 mmol), Ph₃P (6 mg, 0.023 mmol) and (Ph₃P)₄Pd (27 mg, 0.023 mmol). After vacuum-drying, activated 4 Å molecular sieves and piperidine (15 mL) were added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (20 mL) and washed with a saturated solution of NH₄Cl (3 x 15 mL). The organic layer was dried, filtered and concentrated and the residue was purified by flash chromatography (SiO₂, 5% EtOAc/hexanes) to give **3** as a white solid [267 mg, 0.44 mmol, 94%, R_f= 0.59 (20% EtOAc/hexanes)]. ¹H NMR (CDCl₃, 250 MHz): 7.43 (4H, s, Ar), 7.41 (2H, d, *J*=8.3 Hz, Ar) 7.20 (2H, d, *J*=8.3 Hz, Ar), 7.10 (6H, d, *J*=8.8 Hz, Ar), 6.80 (6H, d, *J*=8.8 Hz Ar), 3.80 (9H, s, OMe), 0.27 (9H, s, TMS). ¹³C NMR (CDCl₃, 63 MHz): 157.1 (C), 147.8 (C), 138.6 (C), 131.6 (CH), 131.5 (CH), 130.9 (CH), 130.3 (CH), 123.0 (C), 122.4 (C), 119.9 (C), 112.4 (CH), 104.3 (C), 95.8 (C), 90.9 (C), 88.6 (C), 62.5 (C), 54.8 (CH₃), 0.44 (TMS). MS (EI, *m/z*, %): 606.0 (M⁺, 75), 557.9 (16), 499.0 (M⁺-C₇H₇O, 77), 333.0 (M⁺-C₁₉H₁₇Si, 100). HRMS (EI) calcd. for C₄₁H₃₈O₃Si (M⁺) 606.2590, found 606.2590.

Dendron 4. To a solution of **3** (100 mg, 0.17 mmol) in CH₂Cl₂ (10 mL) and MeOH (4 mL) was added KOH (93 mg, 1.7 mmol) under argon and the mixture was stirred at rt during 1 h. The mixture was concentrated and the residue was dissolved in EtOAc (20 mL). The resulting solution was washed with brine (3x30 mL), dried and concentrated to give a residue that was dissolved in CH₂Cl₂. Precipitation with hexanes gave **4** as a white solid [87 mg, 0.16 mmol, 99%, R_f= 0.48 (20% EtOAc/hexanes)]. ¹H NMR (CDCl₃, 250 MHz): 7.47 (4H, s, Ar), 7.42 (2H, d, *J*=8.2 Hz, Ar), 7.21 (2H, d, *J*=8.2 Hz, Ar), 7.10 (6H, d, *J*=8.7 Hz, Ar_{OMe}), 6.80 (6H, d, *J*=8.7 Hz, Ar_{OMe}), 3.79 (9H, s, OMe), 3.18 (1H, s, C≡C-H). ¹³C NMR (CDCl₃, 63 MHz): 157.1 (C), 147.9 (C), 138.6 (C), 131.6 (CH), 131.5 (CH), 131.0 (CH), 130.6 (CH), 130.3 (CH), 123.4 (C), 121.3 (C), 119.8 (C), 112.3 (CH), 91.0 (C), 88.4 (C), 82.9 (C), 78.5 (C), 62.5 (C), 54.8 (CH₃). MS (EI, *m/z*, %): 534.0 (M⁺, 78), 427.0 (M⁺-C₇H₇O, 85), 333.0 (M⁺-C₁₆H₉, 100). HRMS (EI) calcd. for C₃₈H₃₀O₃ (M⁺) 534.2195, found 534.2195.

Dendrimer G1b. A Schlenk tube equipped with a stirring bar was charged with freshly prepared **4** (176 mg, 0.33 mmol), **5**^{11,13} (60 mg, 0.073 mmol), CuI (6 mg, 0.029 mmol), Ph₃P (8 mg, 0.029 mmol) and (Ph₃P)₄Pd (34 mg, 0.029 mmol). After vacuum-drying, activated 4 Å molecular sieves and piperidine (15 mL) were added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h. Then it was allowed to reach rt to give a white precipitate which was filtered and dissolved in hot CH₂Cl₂ (30 mL). The resulting solution was allowed to slowly reach rt and a white precipitate was formed, which was filtered to give dendrimer **G1b** as a white solid [160 mg, 0.065 mmol, 89%]. ¹H NMR (CDCl₃, 250 MHz): 7.46 (32H, m, Ar), 7.19 (16H, m, Ar), 7.08 (24H, d, *J*=8.7 Hz, Ar_{OMe}), 6.78 (24H, d, *J*=8.8 Hz Ar_{OMe}), 3.79 (36H, s, OMe). ¹³C NMR (CDCl₃, 63 MHz): 157.4 (C), 148.1 (C), 145.8 (C), 138.8 (C), 131.8 (CH), 131.4 (CH), 130.8 (CH), 130.5 (CH), 123.1 (C), 122.7 (C), 121.0 (C), 120.1 (C), 112.6 (CH), 91.1 (C), 90.6 (C), 89.5 (C), 88.9 (C), 64.4 (C), 62.7 (C), 55.0 (CH₃). MS (MALDI-TOF, *m/z*): 2559 (M⁺Ag⁺), 2450 (M⁺), 2343 (M⁺-C₇H₇O), 1840 (M⁺-C₄₄H₃₃O₃).

Trimehyl((4-((4-(*tris*(4-iodophenyl)methyl)phenyl)ethinyl)phenyl)ethinyl)silane (7). A mixture of **6**¹⁴ (77 mg, 0.39 mmol), **5**^{11,13} (400 mg, 0.49 mmol), CuI (9 mg, 0.049 mmol) and (Ph₃P)₄Pd (56 mg, 0.049 mmol) was dissolved in THF (50 mL) by refluxing under argon. Then, the solution was allowed to reach rt and piperidine (0.5 mL, 4.85 mmol) was added. After stirring for 12 h, the mixture was concentrated, the residue was dissolved in CH₂Cl₂ (20 mL) and the resulting solution was washed with a saturated solution of NH₄Cl (3x10 mL). The organic phase was dried and concentrated and the residue was purified by flash chromatography (SiO₂, hexanes) to give **7** as a white solid [139 mg, 0.155 mmol, 30%, R_f= 0.33 (5% CH₂Cl₂/hexanes)]. ¹H NMR (CDCl₃, 250 MHz): 7.59 (6H, d, *J*=8.0 Hz, Ar_I), 7.42 (6H, m, Ar), 7.14 (2H, d, *J*=8.1 Hz, Ar), 6.91 (6H, d, *J*=8.0 Hz Ar_I), 0.27 (9H, s, TMS). ¹³C NMR (CDCl₃, 63 MHz): 145.7 (C), 145.3 (C), 137.2 (CH), 132.8 (CH), 132.0 (CH), 131.5 (CH), 131.3 (CH), 130.8 (CH), 123.2 (C), 123.1 (C), 121.4 (C), 104.7 (C), 96.5 (C), 92.6 (C), 90.8 (C), 89.8 (C), 64.4 (C), 0.08 (TMS). MS (EI, *m/z*, %): 893.2 (M⁺, 100), 690.4 (M⁺-C₆H₅I, 67). HRMS (EI) calcd. For C₄₁H₃₈O₃Si⁺ (M⁺) 893.9173, found 893.9178.

Protected dendron 8. A Schlenk tube equipped with a stirring bar was charged with **4** (330 mg, 0.62 mmol), **7** (158 mg, 0.18 mmol), CuI (5 mg, 0.026 mmol), Ph₃P (7 mg, 0.026 mmol) and (Ph₃P)₄Pd (61 mg, 0.053 mmol). After vacuum-drying, activated 4 Å molecular sieves and piperidine (20 mL) were added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (20 mL) and washed with a saturated solution of NH₄Cl (3 x 15 mL). The organic layer was dried, filtered and concentrated and the residue was purified by flash chromatography (SiO₂, 40% CH₂Cl₂/hexanes) to give **8** as a white solid [260 mg, 0.12 mmol, 70%, R_f= 0.65 (70% toluene/CH₂Cl₂)]. ¹H NMR (CDCl₃, 250 MHz): 7.52-7.35 (30H, m, Ar), 7.21 (14H, m, Ar), 7.10 (18H, d, *J*=8.8 Hz, Ar_{OMe}), 6.80 (18H, d, *J*=8.8 Hz Ar_{OMe}), 3.80 (27H, s, OMe), 0.27 (9H, s, TMS). ¹³C NMR (CDCl₃, 63 MHz): 157.4 (C), 148.1 (C), 145.9 (C), 138.9 (C), 131.8 (CH), 131.4 (CH), 131.0 (CH), 130.9 (CH), 130.8 (CH), 130.5 (CH), 123.1 (C), 122.8 (C), 122.7 (C), 121.1 (C), 120.2 (C), 112.6 (CH), 104.5 (C), 96.2 (C), 91.2 (C), 90.7 (C), 89.5 (C), 88.9 (C), 64.8 (C), 62.8 (C), 55.0 (CH₃), 0.21 (TMS). MS (MALDI-TOF, *m/z*): 2113 (M⁺), 2007 (M⁺-C₇H₇O), 1841 (M⁺-C₁₉H₁₇Si), 1504 (M⁺-C₄₄H₃₃O₃).

Dendron 9. To a solution of **8** (50 mg, 0.024 mmol) in CH₂Cl₂ (5 mL) and MeOH (2 mL) was added KOH (14 mg, 0.24 mmol) under argon and the mixture was stirred at rt during 1 h. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (20 mL). The resulting solution was washed with brine (3x30 mL), dried and concentrated to give a residue that was dissolved in CH₂Cl₂. Precipitation with hexanes gave **9** as a white solid [45 mg, 0.022 mmol, 92%, R_f= 0.6 (30% toluene/CH₂Cl₂)]. This dendron was immediately used in next reaction. ¹H NMR (CDCl₃, 250 MHz): 7.55-7.36 (30H, m, Ar), 7.21 (14H, m, Ar), 7.09 (18H, d, *J*=8.7 Hz, Ar_{OMe}), 6.80 (18H, d, *J*=8.7 Hz, Ar_{OMe}), 3.80 (27H, s, OMe), 3.18 (1H, s, C≡C-H). ¹³C NMR (CDCl₃, 63 MHz): 157.4 (C), 148.1 (C), 145.9 (C), 138.9 (C), 131.9 (CH), 131.8 (CH), 131.4 (CH), 131.0 (CH), 130.9 (CH), 130.8 (CH), 130.5 (CH), 123.9 (C), 123.1 (C), 122.7 (C), 121.8 (C), 121.0 (C), 120.92 (C), 120.2 (C), 112.6 (CH), 91.2 (C), 90.8 (C), 90.6 (C), 89.5 (C), 89.2 (C), 88.9 (C), 83.1 (C), 78.9 (C), 64.8 (C), 62.7 (C), 55.0 (CH₃).

Dendrimer G2b. A Schlenk tube equipped with a stirring bar was charged with freshly prepared **9** (340 mg, 0.17 mmol), **5** (33 mg, 0.037 mmol), CuI (1 mg, 0.0074 mmol), Ph₃P (2 mg, 0.0074 mmol) and (Ph₃P)₄Pd (12 mg, 0.015 mmol). After vacuum-drying, activated 4 Å molecular sieves and piperidine (20 mL) were added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h. Then it was allowed to reach rt. A white precipitate was formed, which was filtered and washed with refluxing CH₂Cl₂/hexanes and EtOAc/hexanes to give **G2b** as a poorly soluble white solid (200 mg, 0.024 mmol, 64%, R_f= 0.54 (20% toluene/CH₂Cl₂). ¹H NMR (CDCl₃, 250 MHz): 7.54-7.36 (128H, m, Ar), 7.19 (64H, m, Ar), 7.08 (72H, d, *J*=7.4 Hz, Ar_{OMe}), 6.79 (72H, d, *J*=7.4 Hz Ar_{OMe}), 3.79 (108H, s, OMe). ¹³C NMR (CDCl₃, 63 MHz): 157.4 (C), 148.1 (C), 145.9 (C), 138.8 (C), 131.8 (CH), 131.4 (CH), 131.0 (CH), 130.9 (CH), 130.7 (CH), 130.5 (CH), 123.1 (C), 122.9 (C), 122.7 (C), 121.0 (C), 120.2 (C), 112.6 (CH), 91.2 (C), 90.9 (C), 90.7 (C), 90.6 (C), 89.5 (C), 88.9 (C), 64.6 (C), 62.7 (C), 55.0 (CH₃). MS (MALDI-TOF, *m/z*): 17074 (M₂Ag⁺), 8591 (MAg⁺), 8375 (M⁺-C₇H₇O), 7872 (M⁺-C₄₄H₃₃O₃).

Protected dendron 12 from 11. A Schlenk tube equipped with a stirring bar was charged with **11**^{11b} (190 mg, 0.24 mmol), **6**¹⁴ (70 mg, 0.36 mmol), CuI (4 mg, 0.047 mmol), Ph₃P (12 mg, 0.024 mmol) and (Ph₃P)₄Pd (27 mg, 0.024 mmol). After vacuum-drying, activated 4 Å molecular sieves and piperidine (15 mL) were added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (30 mL) and washed with a saturated solution of NH₄Cl (3 x 20 mL). The organic layer was dried, filtered and concentrated. The residue was dissolved in CH₂Cl₂, and the product was precipitated with hexanes. The precipitate was filtered and reprecipitated three times to give **12** as a yellow solid [120 mg, 0.14 mmol, 60%]. ¹H NMR (CDCl₃, 250 MHz): 7.41 (4H, s, Ar), 7.36 (2H, d, *J*=7.5 Hz, Ar), 7.28 (6H, d, *J*=7.5 Hz, Ar), 7.22 (2H, d, *J*=7.5 Hz, Ar), 7.16 (6H, d, *J*=7.5 Hz, Ar), 3.73 (12H, s, CH₂-N), 1.66 (18H, s, CH₂), 0.23 (9H, s, TMS). ¹³C NMR (CDCl₃, 63 MHz): 148.5 (C), 147.8 (C), 143.8 (C), 131.7 (CH), 131.5 (CH), 131.2 (CH), 131.1 (CH), 130.5 (CH), 123.3 (C), 122.5 (C), 120.1 (C), 119.3 (CH), 104.6 (C), 95.9 (C), 91.3 (C), 88.7 (C), 63.9 (C), 47.9 (broad,

CH₂-N), 25.1 (CH₂), 24.3 (CH₂), 0.00 (TMS). MS (EI, m/z, %): 849.2 (M⁺, 7), 737.9 (M⁺-C₅H₁₀N₃, 15), 514.9 [M⁺-3x(C₅H₁₀N₃), 100], 438.9 (68). HRMS (EI) calcd. for C₅₃H₅₉N₉Si (M⁺) 849.4663, found 849.4655.

Protected dendron 12 from 10. A Schlenk tube equipped with a stirring bar was charged with **10**^{11b} (88 mg, 0.13 mmol), **2**¹² (66 mg, 0.26 mmol), CuI (3 mg, 0.014 mmol), Ph₃P (7 mg, 0.026 mmol) and (Ph₃P)₄Pd (15 mg, 0.014 mmol). After vacuum-drying, activated 4 Å molecular sieves and piperidine (15 mL) were added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (20 mL) and washed with a saturated solution of NH₄Cl (3 x 10 mL). The organic layer was dried, filtered and concentrated. The residue was dissolved in CH₂Cl₂, and the product was precipitated with hexanes. The precipitate was filtered and reprecipitated three times to give **12** as a yellow solid [90 mg, 0.11 mmol, 81%]. Its spectroscopical data were identical to those of the product obtained from the previous experiment.

Dendron 13. To a solution of **12** (268 mg, 0.32 mmol) in CH₂Cl₂ (15 mL) and MeOH (2 mL) was added KOH (177 mg, 3.15 mmol) under argon and the mixture was stirred at rt during 1 h. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (30 mL) and the solution was washed with brine (3x20 mL), dried and concentrated. The resulting residue was dissolved in CH₂Cl₂ followed by precipitation with hexanes to give **13** as a brown solid [240 mg, 0.31 mmol, 98%, R_f= 0.46 (20% EtOAc/hexanes)]. This dendron was immediately used in next reaction. ¹H NMR (CDCl₃, 250 MHz): 7.50–7.11 (20H, m, Ar), 3.67 (12H, s, CH₂-N), 3.16 (1H, s, C≡C-H), 1.66 (18H, s, CH₂). ¹³C NMR (CDCl₃, 63 MHz): 148.6 (C), 147.9 (C), 143.8 (C), 131.9 (CH), 131.5 (CH), 131.3 (CH), 131.1 (CH), 130.6 (CH), 123.8 (C), 121.6 (C), 120.0 (C), 119.4 (CH), 91.4 (C), 88.6 (C), 83.2 (C), 78.8 (CH), 63.9 (C), 48.1 (broad, CH₂-N), 25.1 (CH₂), 24.3 (CH₂).

Dendrimer G1b-N3. A Schlenk tube equipped with a stirring bar was charged with freshly prepared **13** (240 mg, 0.31 mmol), **5**^{11,13} (56 mg, 0.068 mmol), CuI (5 mg, 0.027 mmol), Ph₃P (11 mg, 0.041 mmol)

and (Ph₃P)₄Pd (32 mg, 0.027 mmol) and then the mixture was dried under vacuum. Activated 4 Å molecular sieves and piperidine (20 mL) were added under argon and the Schlenk tube was sealed with a teflon screw cap. The reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (30 mL) and the solution was washed with a solution of NH₄Cl (3x10mL). The organic phase was dried and concentrated and the residue was purified by column GPC (Bio-Beads S-X1, THF) and precipitation from THF. The precipitate was filtered and washed with refluxing hexanes and then with refluxing MeOH to give **G1b-N3** as a brown solid (150 mg, 0.044 mmol, 64%). ¹H NMR (CDCl₃, 400 MHz): 7.60–7.00 (96H, m, Ar), 3.75 (48H, s, CH₂-N), 1.69 (72H, s, CH₂). ¹³C NMR (CDCl₃, 63 MHz): 148.5 (C), 147.9 (C), 144.1 (CH), 143.8 (CH), 131.5 (CH), 131.0 (CH), 130.5 (CH), 119.3 (CH), 63.9 (C), 48.0 (broad, CH₂-N), 25.1 (CH₂), 24.3 (CH₂).

Dendrimer G1b-I. A Schlenk tube equipped with a stirring bar was charged with **G1b-N3** (70 mg, 0.020 mmol) and it was dried under vacuum. Then, MeI (10 mL) was slowly added under argon, the Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 120 °C during 48 h. After reaching rt, the mixture was diluted with CH₂Cl₂ (50 mL) and the resulting solution was washed with saturated solutions of Na₂S₂O₃ (3x10 mL) and NH₄Cl (3x10 mL). The organic phase was dried and concentrated and the poorly soluble residue was washed with refluxing hexanes and then with MeOH to give **G1b-I** as a yellow solid (70 mg, 0.019 mmol, 95%). ¹H NMR (CDCl₃, 250 MHz): 8.0–7.33 (64H, m, Ar/Ar_I), 7.13 (8H, d, *J*=7.3 Hz, Ar), 6.90 (24H, d, *J*=7.9 Hz, Ar_I). ¹³C NMR (CDCl₃, 63 MHz): 145.0 (C), 136.9 (CH), 132.5 (CH), 131.8 (CH), 131.4 (CH), 131.0 (CH), 130.9 (CH), 130.5 (CH), 129.6 (CH), 92.3 (C), 64.4 (C), 63.7 (C). MS (MALDI-TOF, *m/z*): 2980 (M⁺-C₁₉H₁₂I₃), 2361 [M⁺-2x(C₁₉H₁₂I₃)], 1741 [M⁺-3x(C₁₉H₁₂I₃)].

Dendrimer G1c. Piperidine (0.2 mL, 2.3 mmol) was added to a solution **1**¹¹ (100 mg, 0.23 mmol), CuI (10 mg, 0.46 mmol) and (Ph₃P)₄Pd (5 mg, 0.0046 mmol) in THF (10 mL) and the mixture was stirred at rt for 2 h in an open round bottom flask. The mixture was concentrated, the residue was dissolved in EtOAc (20 mL) and was washed with a solution of NH₄Cl (3x15mL). The organic phase was dried and concentrated and the residue was purified by flash chromatography (SiO₂, 15% EtOAc/hexanes) to give

G1c as a white solid [98 mg, 0.075 mmol, 98%, R_f= 0.4 (30% EtOAc/hexanes)]. ¹H NMR (CDCl₃, 250 MHz): 7.40 (4H, d, *J*=8.4 Hz, Ar), 7.18 (4H, d, *J*=8.4 Hz, Ar), 7.07 (12H, d, *J*=8.9 Hz, Ar_{OMe}), 6.79 (12H, d, *J*=8.9 Hz Ar_{OMe}), 3.79 (18H, s, OMe). ¹³C NMR (CDCl₃, 63 MHz): 157.7 (C), 149.2 (C), 138.9 (C), 132.1 (CH), 131.7 (CH), 131.1 (CH), 119.2 (C), 112.9 (CH), 81.7 (C), 74.0 (C), 63.0 (C), 55.3 (CH₃). **MS** (EI, *m/z*, %): 866 (M⁺, 40), 759 (M⁺-C₇H₇O, 39), 333 (C₂₂H₂₁O₃⁺, 100). **MS** (EI, *m/z*, %): 893.2 (M⁺, 100), 690.4 (M⁺-C₆H₅I, 67). HRMS (EI) calcd. For C₆₀H₅₀O₆⁺ (M⁺) 866.3607, found 866.3607.

Compound 15. A Schlenk tube equipped with a stirring bar was charged with freshly prepared **1**¹¹ (250 mg, 0.58 mmol), **14**⁶ (118 mg, 0.17 mmol), CuI (6 mg, 0.033 mmol), Ph₃P (9 mg, 0.033 mmol) y (Ph₃P)₄Pd (57 mg, 0.050 mmol) and then the mixture was dried under vacuum. Activated 4 Å molecular sieves and piperidine (20 mL) were added under argon and the Schlenk tube was sealed with a teflon screw cap. The reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (20 mL) and the solution was washed with a solution of NH₄Cl (3x15mL). The organic phase was dried and concentrated and the residue was purified by flash chromatography (SiO₂, 30% EtOAc/hexanes) to give **15** as a yellow solid [196 mg, 0.12 mmol, 73%, R_f= 0.42 (40% EtOAc/hexanes)]. ¹H NMR (CDCl₃, 250 MHz): 7.38 (12H, m, Ar), 7.19 (12H, d, *J*=8.3 Hz, Ar), 7.10 (22H, m, Ar_{OMe/OH}), 6.80 (20H, d, *J*=8.7 Hz, Ar_{OMe}), 6.74 (2H, d, *J*=9.1 Hz, Ar_{OH}) 3.80 (27H, s, OMe). ¹³C NMR (CDCl₃, 63 MHz): 157.4 (C), 147.9 (C), 146.4 (C), 138.9 (C), 132.0 (CH), 131.9 (CH), 131.1 (CH), 130.8 (CH), 130.5 (CH), 121.0 (C), 120.4 (C), 112.6 (CH), 89.4 (C), 88.9 (C), 62.6 (C), 55.1 (CH₃). **MS** (MALDI-TOF, *m/z*): 1632.6 (M⁺).

Compound 16. A solution of **15** (120 mg, 0.073 mmol) and Et₃N (0.036 mL, 0.256 mmol) in dry CH₂Cl₂ (20 mL) was cooled to -78 °C during 10 min. Then, Tf₂O (0.024 mL, 0.147 mmol) was added and the mixture was allowed to reach rt for 12 h. The mixture was washed with a saturated solution of NH₄Cl (40 mL) and the aqueous phase was extracted with EtOAc (3x30 mL). The combined organic phase was dried and concentrated and the residue was purified by flash chromatography (SiO₂, 20% EtOAc/hexanes) to give **16** as a white solid [122 mg, 0.069 mmol, 95%, R_f= 0.65 (40% EtOAc/hexanes)]. ¹H NMR (CDCl₃, 250 MHz): 7.46–7.38 (12H, m, Ar), 7.30 (2H, d, *J*=8.9 Hz, Ar_{OTf}), 7.25–7.10 (14H, m, Ar), 7.07 (18H, d,

d, $J=8.9$ Hz, Ar_{OMe}), 6.77 (18H, d, $J=8.9$ Hz, Ar_{OMe}), 3.75 (27H, s, OMe). ¹³C NMR (CDCl₃, 63 MHz): 157.4 (C), 148.0 (C), 145.3 (C), 138.9 (C), 132.5 (CH), 131.8 (CH), 131.1 (CH), 130.8 (CH), 130.5 (CH), 121.5 (C), 120.5 (CH), 120.2 (C), 112.6 (CH), 89.8 (C), 88.5 (C), 62.8 (C), 55.0 (CH₃). MS (MALDI-TOF, m/z): 1764.5 (M⁺).

Protected dendron 17. A Schlenk tube equipped with a stirring bar was charged with **16** (116 g, 0.066 mmol), CuI (1 mg, 0.0066 mmol), Ph₃P (3 mg, 0.0131 mmol) y (Ph₃P)₄Pd (8 mg, 0.0066 mmol). After vacuum-drying, activated 4 Å molecular sieves, trimethylsilylacetylene (0.056 mL, 0.39 mmol) and piperidine (15 mL) were successively added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (20 mL) and washed with a saturated solution of NH₄Cl (3 x 10 mL). The organic layer was dried, filtered and concentrated and the residue was purified by flash chromatography (SiO₂, 20% CH₂Cl₂/hexanes) to give **17**^{1a} as a white solid [107 mg, 0.062 mmol, 95%, R_f= 0.42 (30% EtOAc/hexanes)]. Its spectroscopic data were identical to those of a reference sample.

Dendrimer G2c. Piperidine (0.04 mL, 0.47 mmol) was added to a solution of **18** (153 mg, 0.093 mmol prepared from **17** as previously described by our group^{11a}), CuI (3 mg, 0.19 mmol) and (Ph₃P)₄Pd (22 mg, 0.019 mmol) in THF (10 mL) and the mixture was stirred at rt for 2 h in an open round bottom flask. The mixture was concentrated, the residue was dissolved in EtOAc (20 mL) and was washed with a solution of NH₄Cl (3x15mL). The organic phase was dried and concentrated and the residue was purified by flash chromatography (SiO₂, 25% EtOAc/hexanes) to give **G2c** as a white solid [150 mg, 0.046 mmol, 98%, R_f= 0.45 (80% CH₂Cl₂/hexanes)]. ¹H NMR (CDCl₃, 250 MHz): 7.42 (28H, m, Ar), 7.19 (28H, d, $J=8.1$ Hz, Ar), 7.10 (36H, d, $J=8.8$ Hz, Ar_{OMe}), 6.80 (36H, d, $J=8.8$ Hz Ar_{OMe}), 3.80 (54H, s, OMe). ¹³C NMR (CDCl₃, 63 MHz): 157.6 (C), 148.2 (C), 147.2 (C), 145.7 (C), 139.17 (C), 132.1 (CH), 131.2 (CH), 131.0 (CH), 130.9 (CH), 130.8 (CH), 121.6 (C), 120.6 (C), 119.9 (C), 112.9 (CH), 89.9 (C), 88.9 (C), 81.5 (C), 74.4 (C), 65.0 (C), 62.7 (C), 55.3 (CH₃). MS (MALDI-TOF, m/z): 3389 (M⁺Ag⁺), 3280 (M⁺), 3174 (M⁺-C₇H₇O), 2772 (M⁺-C₃₆H₂₉O₃), 1540 (M⁺-C₁₀₉H₈₇O₉).

Dendrimer G1c-N3. Piperidine (0.110 mL, 1.3 mmol) was added to a solution of **10**^{11b} (88 mg, 0.13 mmol), CuI (50 mg, 0.26 mmol) and (Ph₃P)₄Pd (15 mg, 0.013 mmol) in THF (10 mL) and the mixture was stirred at rt for 2 h in an open round bottom flask. The mixture was concentrated, the residue was dissolved in CH₂Cl₂ (10 mL) and was washed with a solution of NH₄Cl (3x10mL). The organic phase was dried and diluted with hexanes until precipitation of a solid. The precipitate was filtered and dried to give **G1c-N3** (85 mg, 0.063 mmol, 97%). ¹H NMR (CDCl₃, 250 MHz): 7.35 (4H, d, *J*=8.0 Hz, Ar), 7.27 (12H, d, *J*=8.3 Hz, Ar), 7.20 (4H, d, *J*=8.0 Hz, Ar), 7.14 (12H, d, *J*=8.3 Hz, Ar), 3.72 (24H, s, CH₂-N), 1.65 (36H, s, CH₂). ¹³C NMR (CDCl₃, 63 MHz): 148.6 (C), 143.6 (C), 131.4 (CH), 131.0 (CH), 119.4 (CH), 119.0 (C), 81.4 (C), 73.8 (C), 64.0 (C), 48.0 (broad, CH₂-N), 25.1 (CH₂), 24.2 (CH₂).

Dendrimer G1c-I. A Schlenk tube equipped with a stirring bar was charged with **G1c-N3** (8 mg, 0.059 mmol) and it was dried under vacuum. Then, MeI (5 mL) was slowly added under argon, the Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 120 °C during 48 h. After reaching rt, the mixture was diluted with CH₂Cl₂ (50 mL) and the resulting solution was washed with saturated solutions of Na₂S₂O₃ (3x10 mL) and NH₄Cl (3x10 mL). The organic phase was dried and concentrated and the poorly soluble residue was washed with refluxing hexanes and then with MeOH to give **G1c-I** as a yellow solid (70 mg, 0.059 mmol, 82%). ¹H NMR (CDCl₃, 250 MHz): 7.58 (12H, d, *J*=8.5 Hz, Ar_I), 7.41 (4H, d, *J*=8.3 Hz, Ar), 7.11 (4H, d, *J*=8.5 Hz, Ar), 6.88 (12H, d, *J*=8.5 Hz Ar_I).

Dendrimer G3c. A Schlenk tube equipped with a stirring bar was charged with freshly prepared **G1c-I** (15 mg, 0.010 mmol), **18** (152 mg, 0.093 mmol, prepared from **17** as previously described by our group^{11a}), CuI (2 mg, 0.0063 mmol), Ph₃P (2 mg, 0.0063 mmol) y (Ph₃P)₄Pd (8 mg, 0.0073 mmol). After vacuum-drying, activated 4 Å molecular sieves and piperidine (15 mL) were added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The resulting mixture was concentrated and the residue was dissolved in CH₂Cl₂ (20 mL) and washed with a saturated solution of NH₄Cl (3 x 15 mL). The organic layer was dried and concentrated to give a residue, which was purified by column GPC (Bio-Beads SX-1, THF) and precipitation from THF solution. The precipitate was filtered and washed with refluxing hexanes and

methanol to give dendrimer **G3c** as a white solid [88 mg, 0.0084 mmol, 80%, R_f = 0.55 (10% hexanes/CH₂Cl₂)]. ¹H NMR (CDCl₃, 250 MHz): 7.41 (100H, m, Ar), 7.19 (100H, m, CH-Ar), 7.09 (108H, d, *J* = 8.7 Hz, Ar), 6.79 (108H, d, *J* = 8.7 Hz, Ar_{OMe}), 3.78 (162H, s, OMe). ¹³C NMR (CDCl₃, 63 MHz): 157.4 (C), 147.9 (C), 145.9 (C), 145.7 (C), 145.7 (C), 138.9 (C), 131.8 (CH), 130.9 (CH), 130.8 (CH), 130.7 (CH), 130.5 (CH), 121.2 (C), 121.0 (C), 120.3 (C), 112.6 (CH), 89.6 (C), 89.3 (C), 89.1 (C), 88.7 (C), 64.7 (C), 62.7 (C), 55.0 (CH₃). MS (MALDI-TOF, *m/z*): 10636.8 (M^{Ag+}).

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Supporting Information Available: Copies of NMR spectra (PDF).

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Probing the versatility of shape-persistent tetraphenylmethane dendrimers by modification of the skeleton.

Julio I. Urzúa,^{a,†} Sandra Campana,^a Massimo Lazzari^b and Mercedes Torneiro^{a*}

^aDepartamento de Química Orgánica, Facultade de Química, Universidade de Santiago de Compostela, 15782, Santiago de Compostela, Spain.

^bCentro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS) and Departamento de Química Física, Universidade de Santiago de Compostela, 15782, Santiago de Compostela, Spain.

* E-mail: mercedes.torneiro@usc.es

† Present address: Comisión Chilena de Energía Nuclear, calle Nueva Bilbao 12501, Comuna de los Condes, 7600713, Santiago de Chile, Chile.

ABSTRACT. Tetraphenylmethane has emerged as a recurrent building block for advanced porous materials such as COFs, PAFs and hypercrosslinked polymers. Guided by a similar design principle, we have previously synthesized shape-persistent dendrimers with tetraphenylmethane nodes and ethynylene linkers. Here we report the generality of our approach by describing new dendritic architectures built from tetraphenylmethane. First, we prepared expanded dendrimers where the tetrahedral units are bonded through larger rigid rod spacers. Among the different synthetic strategies tested, the convergent route, with alternating steps of Pd-catalyzed Sonogashira coupling and alkyne activation by removal of TMS masking groups, efficiently afforded the first- and second-generation dendrimers. A second type of compounds having a linear diyne at the core is also described. The dendrimers of generations 1-2 were also synthesized by a convergent approach, with the diyne being assembled in the last step of the synthesis by a Glaser oxidative homocoupling of the corresponding dendrons bearing a terminal alkyne at the focal point. A third-generation dendrimer was also successfully prepared by a double-phase strategy.

Introduction

The tetrahedral tetravalent structure of sp^3 carbon is responsible, in conjunction with the diversity of functional groups and the stability of the C-C bond, of the structural and functional variety of organic compounds. Tetraphenylmethane can be considered as an expanded sp^3 carbon that reproduces the same tetrahedral geometry in a larger structure when radially substituted, i.e. at the *para* positions of the aromatic rings. In fact, tetraphenylmethane is a rigid three-dimensional building block widely used to assemble the structural framework of artificial systems of considerable size. To name just a few, it has been employed to build tetrahedral structures,¹ in self-assembled and supramolecular systems,² as

building block for light-emitting and antennae materials,³ in electronically active materials,⁴ in liquid crystals,⁵ for rotaxane stoppers⁶ and as core of shape-persistent dendrimers.⁷ A field of recent development where tetraphenylmethane has been extensively employed is that of organic porous materials. In particular, it has been used as building block for molecular cages,⁸ reticular materials (MOFs and COFs)⁹ and amorphous porous frameworks (microporous polymers, PAFs and related materials).¹⁰ In this last case, the tetraphenylmethane units are hypercrosslinked either directly or through linear spacers to create diamond-related amorphous frameworks with internal voids or pores resulting from the radial stiffness and inefficient packing of the building blocks.

We have recently reported the synthesis and fluorescent properties of shape-persistent dendrimers with tetraphenylmethane nodes and ethynylene linkers of generations 1 and 2 (e.g. **G1a**, Fig. 1).¹¹ The interest of these macromolecules lies in their privileged architectures, with a protein-like globular structure from the second generation. They have a hydrophobic interior with well-defined cavities and the polar terminal groups are effectively located at the periphery with reduced possibilities of backfolding. Being the soluble and structurally-regular analogs of microporous polymers, dendrimers of this type can be potentially used for separation technologies, for gas storage, in catalysis, sensing, and to build multichromophoric luminescent materials or nanomachines.

In this paper, we investigate the scope of the convergent, divergent and double-phase synthetic methodologies to access new members of this family of macromolecules. In addition, we show the versatility of this modular design by preparing dendrimers with modifications at their skeleton, either at the branches or the core. In the first case, our goal is the synthesis of molecules with an expanded structure, which can be accomplished by introducing larger rigid rod linkers between the tetraphenylmethane nodes. As an example, we selected for this work dendrimers **G1b** and **G2b** (Fig. 1),

which have ethynylene-phenylene-ethynylene spacers. As a consequence, they have bigger size and molecular weight than the parent compounds (**G1a** and the analog second-generation dendrimer), while maintaining the shape-persistent structure. Three-dimensional models show that **G1b** has a star-like shape, whereas **G2b** has a globular structure with well-defined inner cavities of bigger volume than the parent compound. On the other side, we also describe in this work dendrimers **G1c**, **G2c** and **G3c** (Fig. 1), with a diyne core. The overall structure is more similar to the related tetraphenylmethane-cored prototypes (e.g. **G1a**), but with an ovoid instead of spherical globular shape resulting from the linear symmetry of the core.

Figure 1. Structure of dendrimers of the **a** (G1a), **b** (G1b, G2b) and **c** series (G1c, G2c, G3c).

Results and Discussion

We started our work with the synthesis of the **b** series macromolecules. We envisaged that the expanded dendrimers could be easily accessed by a convergent route based on Sonogashira Pd-catalyzed couplings, previously demonstrated in our group for the prototype tetraphenylmethane dendrimers with ethynylene linkers.^{11a} The first generation dendron or terminal unit (**4**, Scheme 1) was prepared by coupling of the alkyne **1**¹¹ with the aryl bromide **2**¹² using Pd(PPh₃)₄ as catalyst in the presence of PPh₃,

CuI and 4 Å molecular sieve in piperidine at 100 °C, followed by removal of the TMS group at the focal point by treatment with sodium hydroxide in methanol. A new Sonogashira coupling of the dendron **4** with the core tetraiodide **5**,^{11,13} using the standard preceding conditions, afforded the first-generation dendrimer **G1b** in excellent 83% yield for the three steps.

Scheme 1. Convergent route to dendrimers G1b and G2b.

To address the synthesis of the second-generation dendrimer, we first prepared the branching unit **7** by coupling of the acetylene **6**¹⁴ and the tetraiodide **5** using Pd(PPh₃)₄, PPh₃, CuI and piperidine in THF at rt. The low yield in this reaction (30%) is caused by the statistical reaction of the spacer with the aryl iodides of the tetravalent core. To avoid the formation of undesirable amounts of by-products resulting

from coupling of multiple acetylenes to the core, an excess of the core building block **5** was used, which can be easily separated as the insoluble material in the reaction crude. The Pd-catalyzed coupling of the branching and the terminal units, **7** and **4**, respectively, under standard conditions gave, in good yield, the protected second generation dendron, **8**. Desilylation with NaOH and Sonogashira coupling with the core unit **5** afforded in good yield the second-generation dendrimer **G2b**. **G1b** and **G2b** were fully characterized by MALDI-TOF mass spectrometry and $^1\text{H}/^{13}\text{C}$ NMR spectroscopy and they showed a clean SEC trace with a single peak with retention times according to their molecular weights. A common property of this series of expanded dendrimers is their low solubility, that is useful for their isolation, as they precipitate in the reaction media as white solids. They are very stable, remaining unchanged after several days exposed to air on the bench. In addition, they show a characteristic luminescence that can be observed as a purple glow by illuminating a dilute solution under an UV lamp or as a bright blue spot upon UV irradiation of a sample on a TLC plate. They show a good stability,

Scheme 2. Divergent and double-phase strategies for the b series of dendrimers.

At this point, we decided to apply our recently developed triazene-based divergent route^{11b} to this series of dendrimers for comparative purposes. Therefore, we explored the divergent approach to **G2b** using as starting tetraphenylmethane building blocks the *tris*(triazene) derivatives **10**^{11b} and **11**^{11b} that were coupled to either spacer **2** or **6**, respectively (Scheme 2). In both cases the desired protected expanded dendron **12** was obtained with good to moderate yields. Subsequent desilylation and coupling to tetraiodide **5** afforded the triazene-terminated first generation dendrimer **G1b-N₃** in 63% yield for the two steps, which was transformed in the iodo-terminated dendrimer **G1b-I** by treatment with MeI at 120 °C (95% yield). Unfortunately, our efforts to grow this dendrimer by coupling with dendron **4** were unsuccessful, yielding complex mixtures, in which compound **G2b** could not be detected. The reaction of **G1b-I** with dendron **9** was also tested in an attempt to prepare the corresponding third-generation dendrimer (**G3b**, structure not shown) by a double-stage method, but the desired dendrimer could not be detected in the resulting complex reaction mixtures.

Next, we turned our attention to the synthesis and characterization of the diyne-cored dendrimers of the **c** series. In addition to their interesting structure, these compounds should be easily accessible by Glaser oxidative homocoupling¹⁵ of the corresponding dendrons bearing a terminal alkyne at the focal point. Of the many conditions reported in the literature for this reaction, we selected those that were favorable to the dissolution of the substrates. We started by testing the reaction of **1** with different copper salts as catalyst in CH₂Cl₂,¹⁶ but neither CuI or CuCl in combination with diethylamine, piperidine or pyrrolidine as bases and in the presence of oxygen gave the desired product **G1c**, and the starting material was recovered unaltered. Similar negative results were obtained when the reaction was carried out with Hua's conditions¹⁷ – CuCl and piperidine in toluene.

Scheme 3. Convergent route to dendrimers **G1c** and **G2c**.

Our observation during the synthesis of the tetraphenylmethane-cored dendrimers (e.g. **G1a**) that small amounts of the diyne-cored dendrimers were sometimes obtained as by-products, led us to essay the Sonogashira conditions under air at rt. So, the reaction of **1** with Pd(PPh₃)₄ (0.1 eq.), CuI (0.1 eq.) and piperidine (13 eq.) in THF in the presence of air afforded the desired dendrimer **G1c** in low yield, which was improved to 98% yield by increasing the amount of CuI to 2 eq. (Scheme 3). To undertake the synthesis of the dendrimer **G2c**, we first developed a new synthetic route to the protected second-generation dendron **17**. Instead of coupling the spacer to the tetraiodide **5** with ~30% yield, as in the previously reported method,^{11a} and in the strategy followed to prepare **8** (Scheme 1), we reacted the terminal unit **1** to the known triiodide **14**⁶ to obtain the phenol **15** in 73% yield (Scheme 3). Treatment with triflic anhydride gave the intermediate triflate **16**, which was coupled with the TMSA spacer to yield the desired protected dendron **17** (90% for the two steps). Desilylation to give the dendron **18**^{11a}

followed by Glaser homocoupling in the above optimized conditions afforded the final second-generation dendrimer **G2c** in excellent 96% yield (two steps).

Once demonstrated the feasibility of the convergent method to access the **c** series of dendrimers, we considered worth to attempt the double-stage strategy for the synthesis of a dendrimer of third generation. The Glaser homocoupling of the *tris*(triazene) **10** gave the triazene terminated dendrimer **G1c-N₃** in excellent yield (Scheme 4). Treatment with methyl iodide afforded the hexaiodide **G1c-I** that worked as a supercore for dendrimer growth by Sonogashira reaction with dendron **18**. In this case, the double-stage coupling proceeded smoothly to give the dendrimer **G3c** in 66% yield for the last two steps.

Scheme 4. Double-phase synthesis of G3c.

Dendrimers **G1c**, **G2c** and **G3c** were conveniently characterized (^1H and ^{13}C NMR, MALDI-TOF MS) and showed a clean SEC trace with retention times according to their sizes. They are stable white solids

compounds with good solubility in common solvents (THF, CH₂Cl₂, CHCl₃). By visual inspection they do not show luminiscent properties as in the case of the previous series.

In conclusion, we have shown that tetraphenylmethane-based shape persistent dendrimers have very versatile modular structures that are accessible by different synthetic methodologies. In this work we have prepared two new series of compounds with unique geometrical characteristics, either with a expanded structure or with a diyne core. Both families were easily prepared by a convergent strategy. Whereas the convergent and double-phase routes were unsuccessful for the synthesis of **G2b** and **G3b**, respectively, **G3b** was efficiently prepared by a double-stage methodology. The chemistry involved in those syntheses is basically an iterative process based on Pd-catalyzed Sonogashira couplings of terminal alkynes with aryl iodides and triflates, with alternating steps of activation of masked groups. In the case of the **c** series there is also a key step consisting of a Glaser homodimerization to assemble the core diyne. This is the first example of a double-stage strategy for rigid tetraphenylmethane dendrimers, and also we report the first dendrimer of third generation of this class. Further studies are being carried out in our laboratories to evaluate the properties (e.g. porosity, fluorescence) of these new macromolecular materials, which will be reported in future papers.

Experimental Section¹⁸

Protected dendron 3. A Schlenk tube equipped with a stirring bar was charged with **1**¹¹ (200 mg, 0.46 mmol), **2**¹² (175 mg, 0.69 mmol), CuI (4 mg, 0.023 mmol), Ph₃P (6 mg, 0.023 mmol) and (Ph₃P)₄Pd (27 mg, 0.023 mmol). After vacuum-drying, activated 4 Å molecular sieves and piperidine (15 mL) were added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (20 mL) and washed with a saturated solution of NH₄Cl (3 x 15 mL).

The organic layer was dried, filtered and concentrated and the residue was purified by flash chromatography (SiO₂, 5% EtOAc/hexanes) to give **3** as a white solid [267 mg, 0.44 mmol, 94%, R_f= 0.59 (20% EtOAc/hexanes)]. ¹H NMR (CDCl₃, 250 MHz): 7.43 (4H, s, Ar), 7.41 (2H, d, *J*=8.3 Hz, Ar) 7.20 (2H, d, *J*=8.3 Hz, Ar), 7.10 (6H, d, *J*=8.8 Hz, Ar), 6.80 (6H, d, *J*=8.8 Hz Ar), 3.80 (9H, s, OMe), 0.27 (9H, s, TMS). ¹³C NMR (CDCl₃, 63 MHz): 157.1 (C), 147.8 (C), 138.6 (C), 131.6 (CH), 131.5 (CH), 130.9 (CH), 130.3 (CH), 123.0 (C), 122.4 (C), 119.9 (C), 112.4 (CH), 104.3 (C), 95.8 (C), 90.9 (C), 88.6 (C), 62.5 (C), 54.8 (CH₃), 0.44 (TMS). MS (EI, *m/z*, %): 606.0 (M⁺, 75), 557.9 (16), 499.0 (M⁺-C₇H₇O, 77), 333.0 (M⁺-C₁₉H₁₇Si, 100). HRMS (EI) calcd. for C₄₁H₃₈O₃Si (M⁺) 606.2590, found 606.2590.

Dendron 4. To a solution of **3** (100 mg, 0.17 mmol) in CH₂Cl₂ (10 mL) and MeOH (4 mL) was added KOH (93 mg, 1.7 mmol) under argon and the mixture was stirred at rt during 1 h. The mixture was concentrated and the residue was dissolved in EtOAc (20 mL). The resulting solution was washed with brine (3x30 mL), dried and concentrated to give a residue that was dissolved in CH₂Cl₂. Precipitation with hexanes gave **4** as a white solid [87 mg, 0.16 mmol, 99%, R_f= 0.48 (20% EtOAc/hexanes)]. ¹H NMR (CDCl₃, 250 MHz): 7.47 (4H, s, Ar), 7.42 (2H, d, *J*=8.2 Hz, Ar), 7.21 (2H, d, *J*=8.2 Hz, Ar), 7.10 (6H, d, *J*=8.7 Hz, Ar_{OMe}), 6.80 (6H, d, *J*=8.7 Hz, Ar_{OMe}), 3.79 (9H, s, OMe), 3.18 (1H, s, C≡C-H). ¹³C NMR (CDCl₃, 63 MHz): 157.1 (C), 147.9 (C), 138.6 (C), 131.6 (CH), 131.5 (CH), 131.0 (CH), 130.6 (CH), 130.3 (CH), 123.4 (C), 121.3 (C), 119.8 (C), 112.3 (CH), 91.0 (C), 88.4 (C), 82.9 (C), 78.5 (C), 62.5 (C), 54.8 (CH₃). MS (EI, *m/z*, %): 534.0 (M⁺, 78), 427.0 (M⁺-C₇H₇O, 85), 333.0 (M⁺-C₁₆H₉, 100). HRMS (EI) calcd. for C₃₈H₃₀O₃ (M⁺) 534.2195, found 534.2195.

Dendrimer G1b. A Schlenk tube equipped with a stirring bar was charged with freshly prepared **4** (176 mg, 0.33 mmol), **5**^{11,13} (60 mg, 0.073 mmol), CuI (6 mg, 0.029 mmol), Ph₃P (8 mg, 0.029 mmol)

and (Ph₃P)₄Pd (34 mg, 0.029 mmol). After vacuum-drying, activated 4 Å molecular sieves and piperidine (15 mL) were added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h. Then it was allowed to reach rt to give a white precipitate which was filtered and dissolved in hot CH₂Cl₂ (30 mL). The resulting solution was allowed to slowly reach rt and a white precipitate was formed, which was filtered to give dendrimer **G1b** as a white solid [160 mg, 0.065 mmol, 89%]. ¹H NMR (CDCl₃, 250 MHz): 7.46 (32H, m, Ar), 7.19 (16H, m, Ar), 7.08 (24H, d, *J*=8.7 Hz, Ar_{OMe}), 6.78 (24H, d, *J*=8.8 Hz Ar_{OMe}), 3.79 (36H, s, OMe). ¹³C NMR (CDCl₃, 63 MHz): 157.4 (C), 148.1 (C), 145.8 (C), 138.8 (C), 131.8 (CH), 131.4 (CH), 130.8 (CH), 130.5 (CH), 123.1 (C), 122.7 (C), 121.0 (C), 120.1 (C), 112.6 (CH), 91.1 (C), 90.6 (C), 89.5 (C), 88.9 (C), 64.4 (C), 62.7 (C), 55.0 (CH₃). MS (MALDI-TOF, *m/z*): 2559 (M⁺Ag⁺), 2450 (M⁺), 2343 (M⁺-C₇H₇O), 1840 (M⁺-C₄₄H₃₃O₃).

Trimehyl((4-((4-*tris*(4-iodophenyl)methyl)phenyl)ethinyl)phenyl)ethinyl)silane (7). A mixture of **6**¹⁴ (77 mg, 0.39 mmol), **5**^{11,13} (400 mg, 0.49 mmol), CuI (9 mg, 0.049 mmol) and (Ph₃P)₄Pd (56 mg, 0.049 mmol) was dissolved in THF (50 mL) by refluxing under argon. Then, the solution was allowed to reach rt and piperidine (0.5 mL, 4.85 mmol) was added. After stirring for 12 h, the mixture was concentrated, the residue was dissolved in CH₂Cl₂ (20 mL) and the resulting solution was washed with a saturated solution of NH₄Cl (3x10 mL). The organic phase was dried and concentrated and the residue was purified by flash chromatography (SiO₂, hexanes) to give **7** as a white solid [139 mg, 0.155 mmol, 30%, R_f= 0.33 (5% CH₂Cl₂/hexanes)]. ¹H NMR (CDCl₃, 250 MHz): 7.59 (6H, d, *J*=8.0 Hz, Ar_I), 7.42 (6H, m, Ar), 7.14 (2H, d, *J*=8.1 Hz, Ar), 6.91 (6H, d, *J*=8.0 Hz Ar_I), 0.27 (9H, s, TMS). ¹³C NMR (CDCl₃, 63 MHz): 145.7 (C), 145.3 (C), 137.2 (CH), 132.8 (CH), 132.0 (CH), 131.5 (CH), 131.3 (CH), 130.8 (CH), 123.2 (C), 123.1 (C), 121.4 (C), 104.7 (C), 96.5 (C), 92.6 (C), 90.8 (C), 89.8 (C), 64.4 (C),

0.08 (TMS). MS (EI, m/z, %): 893.2 (M^+ , 100), 690.4 ($M^+ - C_6H_5I$, 67). HRMS (EI) calcd. For $C_{41}H_{38}O_3Si$ (M^+) 893.9173, found 893.9178.

Protected dendron 8. A Schlenk tube equipped with a stirring bar was charged with **4** (330 mg, 0.62 mmol), **7** (158 mg, 0.18 mmol), CuI (5 mg, 0.026 mmol), Ph_3P (7 mg, 0.026 mmol) and $(Ph_3P)_4Pd$ (61 mg, 0.053 mmol). After vacuum-drying, activated 4 Å molecular sieves and piperidine (20 mL) were added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The mixture was concentrated and the residue was dissolved in CH_2Cl_2 (20 mL) and washed with a saturated solution of NH_4Cl (3 x 15 mL). The organic layer was dried, filtered and concentrated and the residue was purified by flash chromatography (SiO_2 , 40% CH_2Cl_2 /hexanes) to give **8** as a white solid [260 mg, 0.12 mmol, 70%, R_f = 0.65 (70% toluene/ CH_2Cl_2)]. 1H NMR ($CDCl_3$, 250 MHz): 7.52-7.35 (30H, m, Ar), 7.21 (14H, m, Ar), 7.10 (18H, d, J =8.8 Hz, Ar_{OMe}), 6.80 (18H, d, J =8.8 Hz Ar_{OMe}), 3.80 (27H, s, OMe), 0.27 (9H, s, TMS). ^{13}C NMR ($CDCl_3$, 63 MHz): 157.4 (C), 148.1 (C), 145.9 (C), 138.9 (C), 131.8 (CH), 131.4 (CH), 131.0 (CH), 130.9 (CH), 130.8 (CH), 130.5 (CH), 123.1 (C), 122.8 (C), 122.7 (C), 121.1 (C), 120.2 (C), 112.6 (CH), 104.5 (C), 96.2 (C), 91.2 (C), 90.7 (C), 89.5 (C), 88.9 (C), 64.8 (C), 62.8 (C), 55.0 (CH_3), 0.21 (TMS). MS (MALDI-TOF, m/z): 2113 (M^+), 2007 ($M^+ - C_7H_7O$), 1841 ($M^+ - C_{19}H_{17}Si$), 1504 ($M^+ - C_{44}H_{33}O_3$).

Dendron 9. To a solution of **8** (50 mg, 0.024 mmol) in CH_2Cl_2 (5 mL) and MeOH (2 mL) was added KOH (14 mg, 0.24 mmol) under argon and the mixture was stirred at rt during 1 h. The mixture was concentrated and the residue was dissolved in CH_2Cl_2 (20 mL). The resulting solution was washed with brine (3x30 mL), dried and concentrated to give a residue that was dissolved in CH_2Cl_2 . Precipitation with hexanes gave **9** as a white solid [45 mg, 0.022 mmol, 92%, R_f = 0.6 (30% toluene/ CH_2Cl_2)]. This

dendron was immediately used in next reaction. ^1H NMR (CDCl_3 , 250 MHz): 7.55-7.36 (30H, m, Ar), 7.21 (14H, m, Ar), 7.09 (18H, d, $J=8.7$ Hz, Ar_{OMe}), 6.80 (18H, d, $J=8.7$ Hz, Ar_{OMe}), 3.80 (27H, s, OMe), 3.18 (1H, s, $\text{C}\equiv\text{C-H}$). ^{13}C NMR (CDCl_3 , 63 MHz): 157.4 (C), 148.1 (C), 145.9 (C), 138.9 (C), 131.9 (CH), 131.8 (CH), 131.4 (CH), 131.0 (CH), 130.9 (CH), 130.8 (CH), 130.5 (CH), 123.9 (C), 123.1 (C), 122.7 (C), 121.8 (C), 121.0 (C), 120.92 (C), 120.2 (C), 112.6 (CH), 91.2 (C), 90.8 (C), 90.6 (C), 89.5 (C), 89.2 (C), 88.9 (C), 83.1 (C), 78.9 (C), 64.8 (C), 62.7 (C), 55.0 (CH_3).

Dendrimer G2b. A Schlenk tube equipped with a stirring bar was charged with freshly prepared **9** (340 mg, 0.17 mmol), **5** (33 mg, 0.037 mmol), CuI (1 mg, 0.0074 mmol), Ph_3P (2 mg, 0.0074 mmol) and $(\text{Ph}_3\text{P})_4\text{Pd}$ (12 mg, 0.015 mmol). After vacuum-drying, activated 4 Å molecular sieves and piperidine (20 mL) were added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h. Then it was allowed to reach rt. A white precipitate was formed, which was filtered and washed with refluxing CH_2Cl_2 /hexanes and EtOAc/hexanes to give **G2b** as a poorly soluble white solid (200 mg, 0.024 mmol, 64%, Rf= 0.54 (20% toluene/ CH_2Cl_2)). ^1H NMR (CDCl_3 , 250 MHz): 7.54-7.36 (128H, m, Ar), 7.19 (64H, m, Ar), 7.08 (72H, d, $J=7.4$ Hz, Ar_{OMe}), 6.79 (72H, d, $J=7.4$ Hz Ar_{OMe}), 3.79 (108H, s, OMe). ^{13}C NMR (CDCl_3 , 63 MHz): 157.4 (C), 148.1 (C), 145.9 (C), 138.8 (C), 131.8 (CH), 131.4 (CH), 131.0 (CH), 130.9 (CH), 130.7 (CH), 130.5 (CH), 123.1 (C), 122.9 (C), 122.7 (C), 121.0 (C), 120.2 (C), 112.6 (CH), 91.2 (C), 90.9 (C), 90.7 (C), 90.6 (C), 89.5 (C), 88.9 (C), 64.6 (C), 62.7 (C), 55.0 (CH_3). MS (MALDI-TOF, m/z): 17074 (M_2Ag^+), 8591 (MAG^+), 8375 ($\text{M}^+-\text{C}_7\text{H}_7\text{O}$), 7872 ($\text{M}^+-\text{C}_{44}\text{H}_{33}\text{O}_3$).

Protected dendron 12 from 11. A Schlenk tube equipped with a stirring bar was charged with **11**^{11b} (190 mg, 0.24 mmol), **6**¹⁴ (70 mg, 0.36 mmol), CuI (4 mg, 0.047 mmol), Ph_3P (12 mg, 0.024 mmol) and $(\text{Ph}_3\text{P})_4\text{Pd}$ (27 mg, 0.024 mmol). After vacuum-drying, activated 4 Å molecular sieves and piperidine

(15 mL) were added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (30 mL) and washed with a saturated solution of NH₄Cl (3 x 20 mL). The organic layer was dried, filtered and concentrated. The residue was dissolved in CH₂Cl₂, and the product was precipitated with hexanes. The precipitate was filtered and reprecipitated three times to give **12** as a yellow solid [120 mg, 0.14 mmol, 60%]. ¹H NMR (CDCl₃, 250 MHz): 7.41 (4H, s, Ar), 7.36 (2H, d, *J*=7.5 Hz, Ar), 7.28 (6H, d, *J*=7.5 Hz, Ar), 7.22 (2H, d, *J*=7.5 Hz, Ar), 7.16 (6H, d, *J*=7.5 Hz, Ar), 3.73 (12H, s, CH₂-N), 1.66 (18H, s, CH₂), 0.23 (9H, s, TMS). ¹³C NMR (CDCl₃, 63 MHz): 148.5 (C), 147.8 (C), 143.8 (C), 131.7 (CH), 131.5 (CH), 131.2 (CH), 131.1 (CH), 130.5 (CH), 123.3 (C), 122.5 (C), 120.1 (C), 119.3 (CH), 104.6 (C), 95.9 (C), 91.3 (C), 88.7 (C), 63.9 (C), 47.9 (broad, CH₂-N), 25.1 (CH₂), 24.3 (CH₂), 0.00 (TMS). MS (EI, *m/z*, %): 849.2 (M⁺, 7), 737.9 (M⁺-C₅H₁₀N₃, 15), 514.9 [M⁺-3x(C₅H₁₀N₃), 100], 438.9 (68). HRMS (EI) calcd. for C₅₃H₅₉N₉Si (M⁺) 849.4663, found 849.4655.

Protected dendron 12 from 10. A Schlenk tube equipped with a stirring bar was charged with **10**^{11b} (88 mg, 0.13 mmol), **2**¹² (66 mg, 0.26 mmol), CuI (3 mg, 0.014 mmol), Ph₃P (7 mg, 0.026 mmol) and (Ph₃P)₄Pd (15 mg, 0.014 mmol). After vacuum-drying, activated 4 Å molecular sieves and piperidine (15 mL) were added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (20 mL) and washed with a saturated solution of NH₄Cl (3 x 10 mL). The organic layer was dried, filtered and concentrated. The residue was dissolved in CH₂Cl₂, and the product was precipitated with hexanes. The precipitate was filtered and reprecipitated

three times to give **12** as a yellow solid [90 mg, 0.11 mmol, 81%]. Its spectroscopical data were identical to those of the product obtained from the previous experiment.

Dendron 13. To a solution of **12** (268 mg, 0.32 mmol) in CH₂Cl₂ (15 mL) and MeOH (2 mL) was added KOH (177 mg, 3.15 mmol) under argon and the mixture was stirred at rt during 1 h. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (30 mL) and the solution was washed with brine (3x20 mL), dried and concentrated. The resulting residue was dissolved in CH₂Cl₂ followed by precipitation with hexanes to give **13** as a brown solid [240 mg, 0.31 mmol, 98%, R_f= 0.46 (20% EtOAc/hexanes)]. This dendron was immediately used in next reaction. ¹H NMR (CDCl₃, 250 MHz): 7.50–7.11 (20H, m, Ar), 3.67 (12H, s, CH₂-N), 3.16 (1H, s, C≡C-H), 1.66 (18H, s, CH₂). ¹³C NMR (CDCl₃, 63 MHz): 148.6 (C), 147.9 (C), 143.8 (C), 131.9 (CH), 131.5 (CH), 131.3 (CH), 131.1 (CH), 130.6 (CH), 123.8 (C), 121.6 (C), 120.0 (C), 119.4 (CH), 91.4 (C), 88.6 (C), 83.2 (C), 78.8 (CH), 63.9 (C), 48.1 (broad, CH₂-N), 25.1 (CH₂), 24.3 (CH₂).

Dendrimer G1b-N3. A Schlenk tube equipped with a stirring bar was charged with freshly prepared **13** (240 mg, 0.31 mmol), **5**^{11,13} (56 mg, 0.068 mmol), CuI (5 mg, 0.027 mmol), Ph₃P (11 mg, 0.041 mmol) and (Ph₃P)₄Pd (32 mg, 0.027 mmol) and then the mixture was dried under vacuum. Activated 4 Å molecular sieves and piperidine (20 mL) were added under argon and the Schlenk tube was sealed with a teflon screw cap. The reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (30 mL) and the solution was washed with a solution of NH₄Cl (3x10mL). The organic phase was dried and concentrated and the residue was purified by column GPC (Bio-Beads S-X1, THF) and precipitation from THF. The precipitate was filtered and washed with refluxing hexanes and then with refluxing MeOH to give **G1b-N3** as a brown solid (150 mg, 0.044 mmol, 64%). ¹H NMR (CDCl₃, 400 MHz): 7.60–7.00 (96H, m, Ar),

3.75 (48H, s, CH₂-N), 1.69 (72H, s, CH₂). ¹³C NMR (CDCl₃, 63 MHz): 148.5 (C), 147.9 (C), 144.1 (CH), 143.8 (CH), 131.5 (CH), 131.0 (CH), 130.5 (CH), 119.3 (CH), 63.9 (C), 48.0 (broad, CH₂-N), 25.1 (CH₂), 24.3 (CH₂).

Dendrimer G1b-I. A Schlenk tube equipped with a stirring bar was charged with **G1b-N3** (70 mg, 0.020 mmol) and it was dried under vacuum. Then, MeI (10 mL) was slowly added under argon, the Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 120 °C during 48 h. After reaching rt, the mixture was diluted with CH₂Cl₂ (50 mL) and the resulting solution was washed with saturated solutions of Na₂S₂O₃ (3x10 mL) and NH₄Cl (3x10 mL). The organic phase was dried and concentrated and the poorly soluble residue was washed with refluxing hexanes and then with MeOH to give **G1b-I** as a yellow solid (70 mg, 0.019 mmol, 95%). ¹H NMR (CDCl₃, 250 MHz): 8.0–7.33 (64H, m, Ar/Ar_I), 7.13 (8H, d, *J*=7.3 Hz, Ar), 6.90 (24H, d, *J*=7.9 Hz, Ar_I). ¹³C NMR (CDCl₃, 63 MHz): 145.0 (C), 136.9 (CH), 132.5 (CH), 131.8 (CH), 131.4 (CH), 131.0 (CH), 130.9 (CH), 130.5 (CH), 129.6 (CH), 92.3 (C), 64.4 (C), 63.7 (C). MS (MALDI-TOF, *m/z*): 2980 (M⁺-C₁₉H₁₂I₃), 2361 [M⁺-2x(C₁₉H₁₂I₃)], 1741 [M⁺-3x(C₁₉H₁₂I₃)].

Dendrimer G1c. Piperidine (0.2 mL, 2.3 mmol) was added to a solution **1**¹¹ (100 mg, 0.23 mmol), CuI (10 mg, 0.46 mmol) and (Ph₃P)₄Pd (5 mg, 0.0046 mmol) in THF (10 mL) and the mixture was stirred at rt for 2 h in an open round bottom flask. The mixture was concentrated, the residue was dissolved in EtOAc (20 mL) and was washed with a solution of NH₄Cl (3x15mL). The organic phase was dried and concentrated and the residue was purified by flash chromatography (SiO₂, 15% EtOAc/hexanes) to give **G1c** as a white solid [98 mg, 0.075 mmol, 98%, R_f= 0.4 (30% EtOAc/hexanes)]. ¹H NMR (CDCl₃, 250 MHz): 7.40 (4H, d, *J*=8.4 Hz, Ar), 7.18 (4H, d, *J*=8.4 Hz, Ar), 7.07 (12H, d, *J*=8.9 Hz, Ar_{OMe}), 6.79 (12H, d, *J*=8.9 Hz Ar_{OMe}), 3.79 (18H, s, OMe). ¹³C NMR (CDCl₃,

63 MHz): 157.7 (C), 149.2 (C), 138.9 (C), 132.1 (CH), 131.7 (CH), 131.1 (CH), 119.2 (C), 112.9 (CH), 81.7 (C), 74.0 (C), 63.0 (C), 55.3 (CH₃). MS (EI, m/z, %): 866 (M⁺, 40), 759 (M⁺-C₇H₇O, 39), 333 (C₂₂H₂₁O₃⁺, 100). MS (EI, m/z, %): 893.2 (M⁺, 100), 690.4 (M⁺-C₆H₅I, 67). HRMS (EI) calcd. For C₆₀H₅₀O₆⁺ (M⁺) 866.3607, found 866.3607.

Compound 15. A Schlenk tube equipped with a stirring bar was charged with freshly prepared **1**¹¹ (250 mg, 0.58 mmol), **14**⁶ (118 mg, 0.17 mmol), CuI (6 mg, 0.033 mmol), Ph₃P (9 mg, 0.033 mmol) y (Ph₃P)₄Pd (57 mg, 0.050 mmol) and then the mixture was dried under vacuum. Activated 4 Å molecular sieves and piperidine (20 mL) were added under argon and the Schlenk tube was sealed with a teflon screw cap. The reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (20 mL) and the solution was washed with a solution of NH₄Cl (3x15mL). The organic phase was dried and concentrated and the residue was purified by flash chromatography (SiO₂, 30% EtOAc/hexanes) to give **15** as a yellow solid [196 mg, 0.12 mmol, 73%, R_f= 0.42 (40% EtOAc/hexanes)]. ¹H NMR (CDCl₃, 250 MHz): 7.38 (12H, m, Ar), 7.19 (12H, d, J=8.3 Hz, Ar), 7.10 (22H, m, Ar_{OMe/OH}), 6.80 (20H, d, J=8.7 Hz, Ar_{OMe}), 6.74 (2H, d, J=9.1 Hz, Ar_{OH}) 3.80 (27H, s, OMe). ¹³C NMR (CDCl₃, 63 MHz): 157.4 (C), 147.9 (C), 146.4 (C), 138.9 (C), 132.0 (CH), 131.9 (CH), 131.1 (CH), 130.8 (CH), 130.5 (CH), 121.0 (C), 120.4 (C), 112.6 (CH), 89.4 (C), 88.9 (C), 62.6 (C), 55.1 (CH₃). MS (MALDI-TOF, m/z): 1632.6 (M⁺).

Compound 16. A solution of **15** (120 mg, 0.073 mmol) and Et₃N (0.036 mL, 0.256 mmol) in dry CH₂Cl₂ (20 mL) was cooled to -78 °C during 10 min. Then, Tf₂O (0.024 mL, 0.147 mmol) was added and the mixture was allowed to reach rt for 12 h. The mixture was washed with a saturated solution of NH₄Cl (40 mL) and the aqueous phase was extracted with EtOAc (3x30 mL). The combined organic phase was dried and concentrated and the residue was purified by flash chromatography (SiO₂, 20%

EtOAc/hexanes) to give **16** as a white solid [122 mg, 0.069 mmol, 95%, Rf= 0.65 (40% EtOAc/hexanes)]. ¹H NMR (CDCl₃, 250 MHz): 7.46–7.38 (12H, m, Ar), 7.30 (2H, d, *J*=8.9 Hz, Ar_{OTf}), 7.25–7.10 (14H, m, Ar), 7.07 (18H, d, d, *J*=8.9 Hz, Ar_{OMe}), 6.77 (18H, d, *J*=8.9 Hz, Ar_{OMe}), 3.75 (27H, s, OMe). ¹³C NMR (CDCl₃, 63 MHz): 157.4 (C), 148.0 (C), 145.3 (C), 138.9 (C), 132.5 (CH), 131.8 (CH), 131.1 (CH), 130.8 (CH), 130.5 (CH), 121.5 (C), 120.5 (CH), 120.2 (C), 112.6 (CH), 89.8 (C), 88.5 (C), 62.8 (C), 55.0 (CH₃). MS (MALDI-TOF, *m/z*): 1764.5 (M⁺).

Protected dendron 17. A Schlenk tube equipped with a stirring bar was charged with **16** (116 g, 0.066 mmol), CuI (1 mg, 0.0066 mmol), Ph₃P (3 mg, 0.0131 mmol) y (Ph₃P)₄Pd (8 mg, 0.0066 mmol). After vacuum-drying, activated 4 Å molecular sieves, trimethylsilylacetylene (0.056 mL, 0.39 mmol) and piperidine (15 mL) were successively added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The mixture was concentrated and the residue was dissolved in CH₂Cl₂ (20 mL) and washed with a saturated solution of NH₄Cl (3 x 10 mL). The organic layer was dried, filtered and concentrated and the residue was purified by flash chromatography (SiO₂, 20% CH₂Cl₂/hexanes) to give **17**^{11a} as a white solid [107 mg, 0.062 mmol, 95%, Rf= 0.42 (30% EtOAc/hexanes)]. Its spectroscopic data were identical to those of a reference sample.

Dendrimer G2c. Piperidine (0.04 mL, 0.47 mmol) was added to a solution of **18** (153 mg, 0.093 mmol prepared from **17** as previously described by our group^{11a}), CuI (3 mg, 0.19 mmol) and (Ph₃P)₄Pd (22 mg, 0.019 mmol) in THF (10 mL) and the mixture was stirred at rt for 2 h in an open round bottom flask. The mixture was concentrated, the residue was dissolved in EtOAc (20 mL) and was washed with a solution of NH₄Cl (3x15mL). The organic phase was dried and concentrated and the residue was purified by flash chromatography (SiO₂, 25% EtOAc/hexanes) to give **G2c** as a white solid [150 mg,

0.046 mmol, 98%, Rf= 0.45 (80% CH₂Cl₂/hexanes)]. ¹H NMR (CDCl₃, 250 MHz): 7.42 (28H, m, Ar), 7.19 (28H, d, *J*=8.1 Hz, Ar), 7.10 (36H, d, *J*=8.8 Hz, Ar_{OMe}), 6.80 (36H, d, *J*=8.8 Hz Ar_{OMe}), 3.80 (54H, s, OMe). ¹³C NMR (CDCl₃, 63 MHz): 157.6 (C), 148.2 (C), 147.2 (C), 145.7 (C), 139.17 (C), 132.1 (CH), 131.2 (CH), 131.0 (CH), 130.9 (CH), 130.8 (CH), 121.6 (C), 120.6 (C), 119.9 (C), 112.9 (CH), 89.9 (C), 88.9 (C), 81.5 (C), 74.4 (C), 65.0 (C), 62.7 (C), 55.3 (CH₃). MS (MALDI-TOF, *m/z*): 3389 (M⁺Ag⁺), 3280 (M⁺), 3174 (M⁺-C₇H₇O), 2772 (M⁺-C₃₆H₂₉O₃), 1540 (M⁺-C₁₀₉H₈₇O₉).

Dendrimer G1c-N3. Piperidine (0.110 mL, 1.3 mmol) was added to a solution of **10**^{11b} (88 mg, 0.13 mmol), CuI (50 mg, 0.26 mmol) and (Ph₃P)₄Pd (15 mg, 0.013 mmol) in THF (10 mL) and the mixture was stirred at rt for 2 h in an open round bottom flask. The mixture was concentrated, the residue was dissolved in CH₂Cl₂ (10 mL) and was washed with a solution of NH₄Cl (3x10mL). The organic phase was dried and diluted with hexanes until precipitation of a solid. The precipitate was filtered and dried to give **G1c-N3** (85 mg, 0.063 mmol, 97%). ¹H NMR (CDCl₃, 250 MHz): 7.35 (4H, d, *J*=8.0 Hz, Ar), 7.27 (12H, d, *J*=8.3 Hz, Ar), 7.20 (4H, d, *J*=8.0 Hz, Ar), 7.14 (12H, d, *J*=8.3 Hz, Ar), 3.72 (24H, s, CH₂-N), 1.65 (36H, s, CH₂). ¹³C NMR (CDCl₃, 63 MHz): 148.6 (C), 143.6 (C), 131.4 (CH), 131.0 (CH), 119.4 (CH), 119.0 (C), 81.4 (C), 73.8 (C), 64.0 (C), 48.0 (broad, CH₂-N), 25.1 (CH₂), 24.2 (CH₂).

Dendrimer G1c-I. A Schlenk tube equipped with a stirring bar was charged with **G1c-N3** (8 mg, 0.059 mmol) and it was dried under vacuum. Then, MeI (5 mL) was slowly added under argon, the Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 120 °C during 48 h. After reaching rt, the mixture was diluted with CH₂Cl₂ (50 mL) and the resulting solution was washed with saturated solutions of Na₂S₂O₃ (3x10 mL) and NH₄Cl (3x10 mL). The organic phase was dried and concentrated and the poorly soluble residue was washed with refluxing hexanes and then with MeOH to give **G1c-I** as a yellow solid (70 mg, 0.059 mmol, 82%). ¹H NMR (CDCl₃, 250 MHz): 7.58

(12H, d, $J=8.5$ Hz, Ar_I), 7.41 (4H, d, $J=8.3$ Hz, Ar), 7.11 (4H, d, $J=8.5$ Hz, Ar), 6.88 (12H, d, $J=8.5$ Hz, Ar_I).

Dendrimer G3c. A Schlenk tube equipped with a stirring bar was charged with freshly prepared **G1c-I** (15 mg, 0.010 mmol), **18** (152 mg, 0.093 mmol, prepared from **17** as previously described by our group^{11a}), CuI (2 mg, 0.0063 mmol), Ph₃P (2 mg, 0.0063 mmol) y (Ph₃P)₄Pd (8 mg, 0.0073 mmol). After vacuum-drying, activated 4 Å molecular sieves and piperidine (15 mL) were added under argon. The Schlenk tube was sealed with a teflon screw cap and the reaction mixture was stirred at 100 °C during 12 h and then it was allowed to reach rt. The resulting mixture was concentrated and the residue was dissolved in CH₂Cl₂ (20 mL) and washed with a saturated solution of NH₄Cl (3 x 15 mL). The organic layer was dried and concentrated to give a residue, which was purified by column GPC (Bio-Beads SX-1, THF) and precipitation from THF solution. The precipitate was filtered and washed with refluxing hexanes and methanol to give dendrimer **G3c** as a white solid [88 mg, 0.0084 mmol, 80%, R_f= 0.55 (10% hexanes/ CH₂Cl₂)]. ¹H NMR (CDCl₃, 250 MHz): 7.41 (100H, m, Ar), 7.19 (100H, m, CH-Ar), 7.09 (108H, d, $J=8.7$ Hz, Ar), 6.79 (108H, d, $J=8.7$ Hz, Ar_{OMe}), 3.78 (162H, s, OMe). ¹³C NMR (CDCl₃, 63 MHz): 157.4 (C), 147.9 (C), 145.9 (C), 145.7 (C), 145.7 (C), 138.9 (C), 131.8 (CH), 130.9 (CH), 130.8 (CH), 130.7 (CH), 130.5 (CH), 121.2 (C), 121.0 (C), 120.3 (C), 112.6 (CH), 89.6 (C), 89.3 (C), 89.1 (C), 88.7 (C), 64.7 (C), 62.7 (C), 55.0 (CH₃). MS (MALDI-TOF, m/z): 10636.8 (M⁺Ag⁺).

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Supporting Information Available: Copies of NMR spectra (PDF).

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