New pyridylphenylene cyclopentadienon as a building block for dendrimer synthesis

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The synthesis of new tetrasubstituted pyridyl-containing cyclopentadienone, namely, 3,4-bis(4-(phenylethynyl)phenyl)-2,5-di(pyridin-2-yl)cyclopenta-2,4-dien-1-one is reported for the first time as a monomer for dendrimer synthesis. The synthesis by Diels—Alder approach allowed to prepare 2nd generation dendrimer with phenylethynyl peripherial fragments. A presence of triple bonds in the structure of dendrimers determines the possibility of their subsequent modification, in particular, by coordinating with metal compounds to obtain catalytically active nanocomposites.

Key words: pyridylphenylene dendrimers, Knoevenagel condensation, functional ligand.

Dendrimers are hyperbranched macromolecules with a well-defined structure and specific topology, which determines the possibility of stabilization of nanoparticles due to encapsulation or interaction with peripheral groups. Previously, stabilization of catalytically active nanoparticles was often carried out by polymers containing heteroatoms. This approach was actively used in the 90′s of the last century.[1—5] The advantage of dendrimers over polymers is in their well-defined and specific architecture, which makes it possible to choose the dendrimer generation and the position of the metal precursor. This subsequently influences the formation of a nanoparticle. Dendrimer-stabilized nanoparticles can be used both in heterogeneous and homogeneous catalysis. The correct choice of the peripheral groups of the dendrimer responsible for its solubility in suitable solvents (dichloromethane, chloroform, tetrahydrofuran, *N*-methyl-2-pyrrolidone) is necessary for homogeneous catalysis. In case of heterogeneous catalysis dendrimers with nanoparticles are immobilized on a solid support, or nanoparticles are formed after fixing the dendrimer on a carrier. However, the presence of functional groups capable for coordinating with metal compounds in the structure of the dendrimer is necessary.

Earlier, we carried out a series of works on the formation of catalytic and magnetic nanoparticles in the presence of aromatic pyridyl-containing dendrimers and dendrons of various generations.[6—10] Obtained results were promising and allowed to synthesize effective catalysts for different reactions.[11—13] In this work, we develop the idea of creating functional dendrimers for catalytic applications using the example of the synthesis of an aromatic dendrimer that contains both pyridyl groups for effective coordination with metal compounds and phenylacetylene fragments at the periphery of the dendrimer molecule that are capable of post-modification.

Results and Discussion

The synthesis of AB_2 monomer was carried out in two steps according to Scheme 1. First, palladium-catalyzed cross-coupling (Sonogashira reaction) of 1,2-bis(4-bromophenyl)ethane-1,2-dione (**1**) with phenylacetylene (**2**) afforded 1,2-bis[4-(phenylethynyl) phenyl]ethan-1,2-dione (**3**). Then 4-hydroxy-3,4-bis[4-(phenylethynyl)-phenyl]-2,5-di(pyridin-2-yl)cyclopent-2-en-1-one (**5**) was synthesized by Knoevenagel condensation of diketone **3** with 1,3-di(pyridin-2-yl)propan-2-one (**4**). As a next step, 3,4-bis[4- (phenylethinyl)phenyl]-2,5-di(pyridin-2-yl)cyclopenta-2,4-dien-1-one (**6**) was obtained from **5**.

The Knoevenagel reaction is widely applied for the synthesis of cyclopentadienones. This determined the choice of the synthesis method of the building block, namely, a monomer of the type AB_2. We previously used this technique for the synthesis of a variety of tetra-substituted aromatic cyclopentadienones in the preparation of dendrimers.[9] The enol form of compound **6**, namely, enolone **5** is formed as the main product under the conditions of the reaction. It was found that the elimination of

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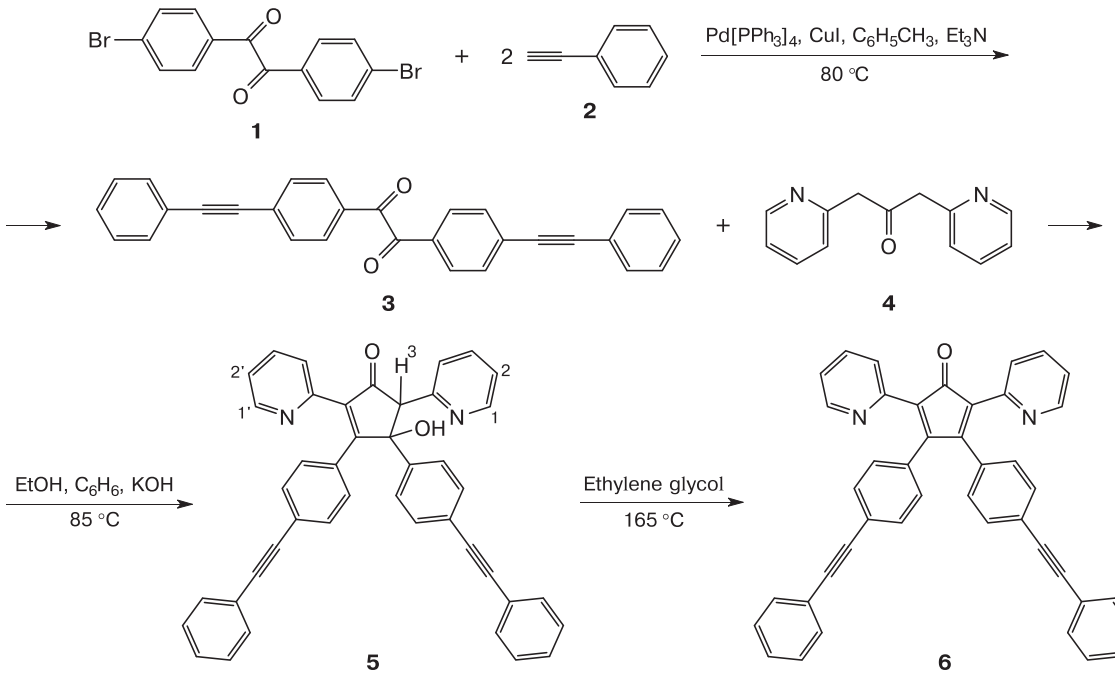
Scheme 1



water to form the desired 3,4-bis[4-(phenylethinyl)-phenyl]-2.5-di(pyridin-2-yl)cyclopenta-2,4-dien-1-one (**6**) occurs in ethylene glycol at 165 °C. At the same time, we have previously shown that the enol form can be converted into the corresponding cyclopentadienone *in situ* under the conditions of the Diels—Alder reaction in the synthesis of dendrimers.[14] We also used the enol form of compound **6** in order to simplify the dendrimer synthesis in this work.

Typical scheme for the synthesis of cyclopentadienones by the Knoevenagel reaction was modified to increase the yield of the product from 35 to 85%. The initial low yield of compound **5** was due to the poor solubility of the starting diketone **3** in ethanol. In this regard, we used benzene as a co-solvent. In addition, the gradual introduction of the catalyst (a solution of KOH in ethanol) dropwise also led to an increase in the product yield.

The structure of the obtained enolone **5** was confirmed by ^{1}H NMR spectroscopy. The spectrum of the compound contains doublets at δ 8.70 and 8.56, corresponding to the H(1) and H(1′) atoms of nonequivalent pyridine fragments. Triplets in the intervals of chemical shifts δ of 7.63—7.67 and 7.74—7.78 corresponding to the H(2) and H(2′) atoms of the pyridine rings are also present. In addition, the characteristic singlet of the H(3) atom of the enol form at δ 4.18 is found. The molecular weight of compound **6** was found by electron impact ionization and corresponded to the calculated value (587 g mol^{-1}).

The synthesis of pyridylphenylene dendrimer **7** was carried out according to divergent Scheme 2 using a trifunctional branching center (1,3,5-triethinylbenzene) and a sequence of two reactions, namely, [2+4] cycloaddition and desilylation. Previously developed synthetic scheme[14] made it possible to afford a high-purity dendrimer (100% according to GPC data) in 77% yield.

The synthesized pyridylphenylene dendrimer **7** interacted with an 1.5-fold excess of 3,4-bis[4-(phenylethynyl) phenyl]-2,5-di(pyridin-2-yl)cyclopenta-2,4-dien-1-one (**6**) formed *in situ* from enolone **5** according to Scheme 3. According to MALDI-TOF mass spectrometry (Fig. 1) and GPC analysis (Fig. 2), the excess of cyclopentadienone **6** interacts with the acetylene groups of the phenylacetylene fragment affording in addition to dendrimer **8** with a molecular weight of 4721 g mol^{-1} a by-product with a molecular weight of 5280 g mol^{-1} (structure **8a**).

The optimal reaction time was found to be 9.5 h. Reaction resulted in complete conversion of terminal

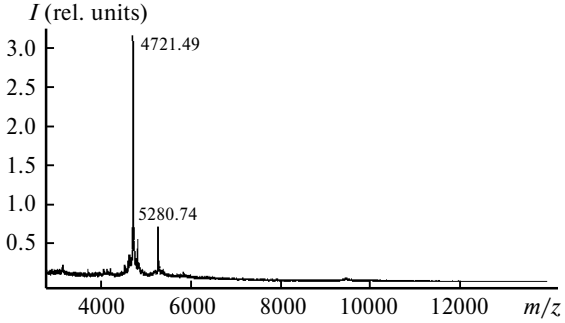
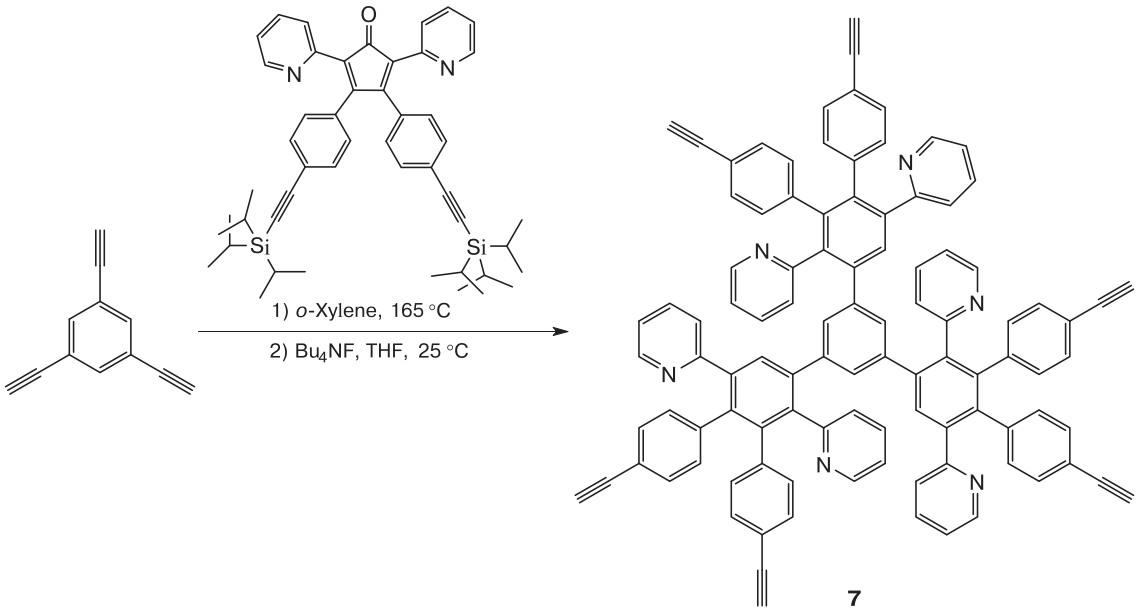


Fig. 1. MALDI-TOF mass spectrum of dendrimer **8** and by-product **8a**.

Scheme 2



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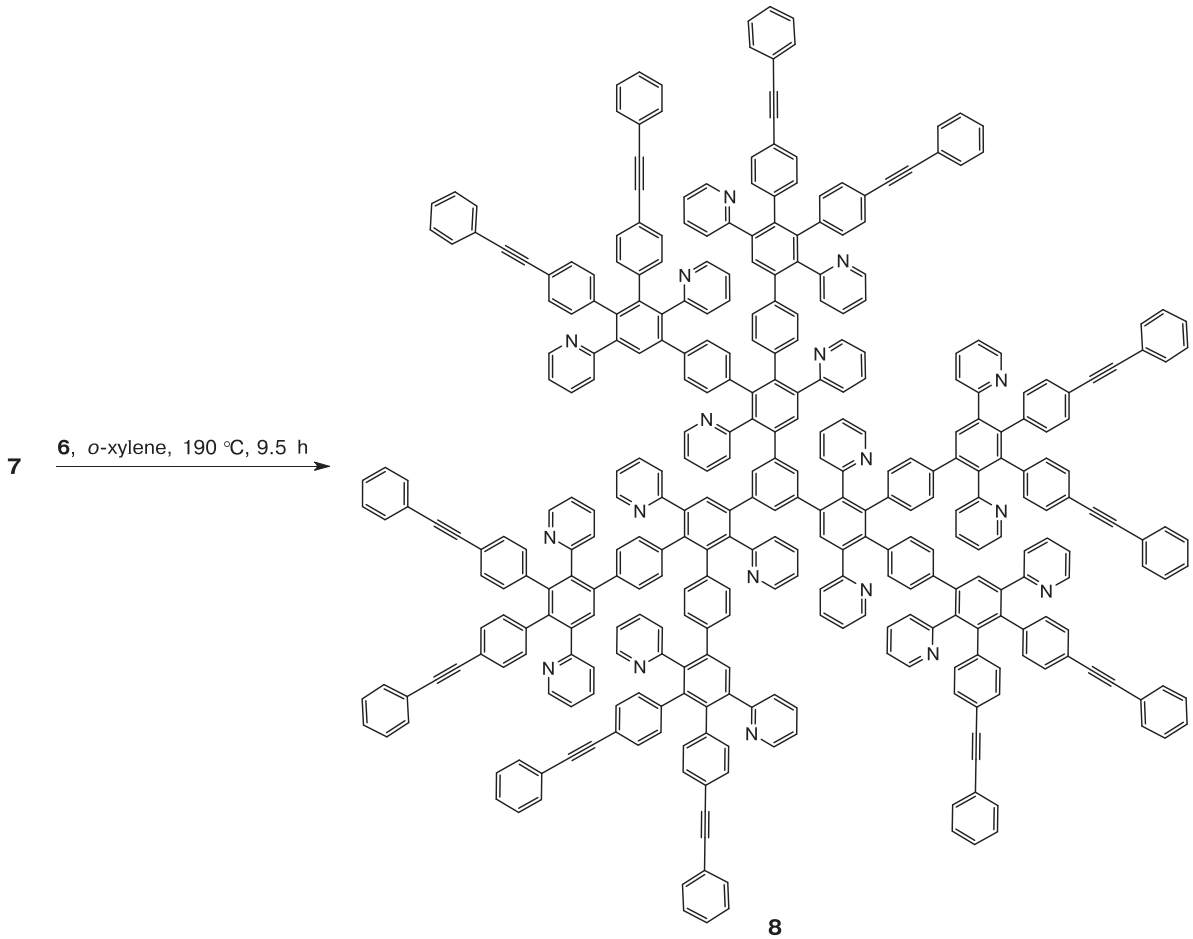
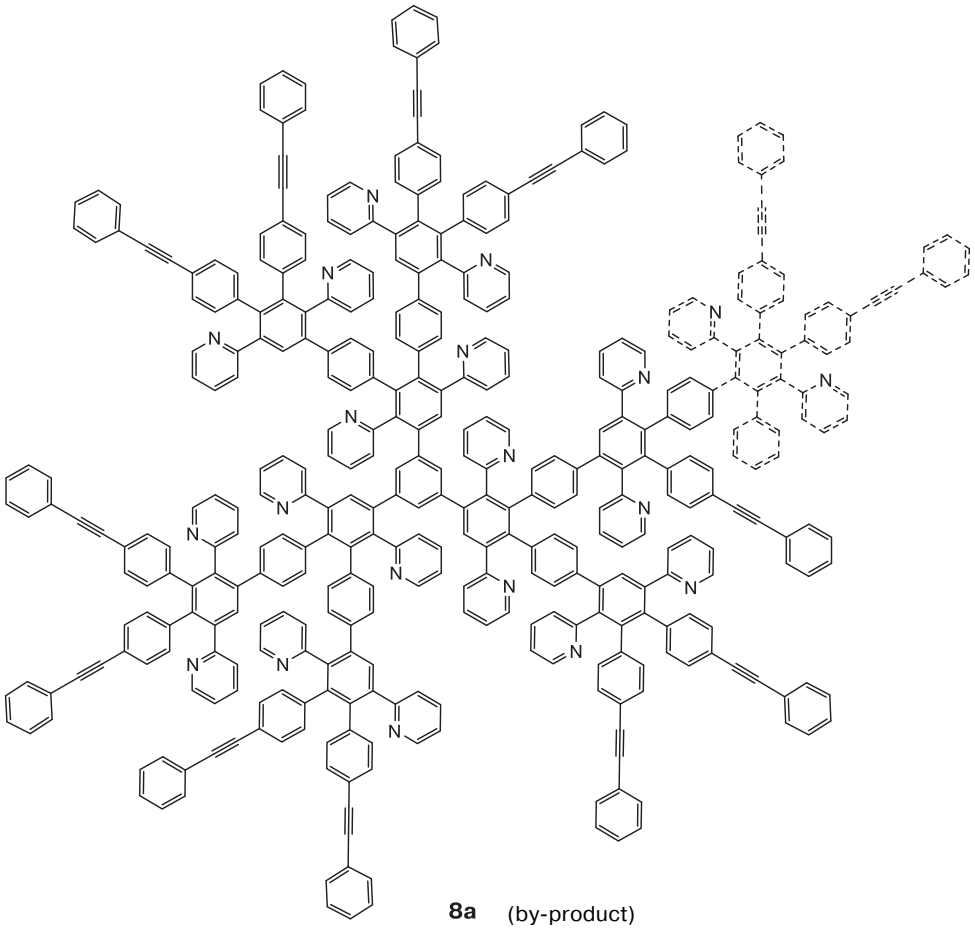
Scheme 3



8



8a (by-product)

ethynyl groups without formation of any by-products. Dendrimer **8** was 100% pure according to GPC (see Fig. 2, line 2).

An additional confirmation of the purity of the synthesized dendrimer was the mass spectrum of product **8** (Fig. 3) obtained by the MALDI-TOF method. The signal corresponds to the calculated molecular weight of the dendrimer (4721 g mol^{-1}).

Thus, we synthesized a new pyridylphenylene cyclopentadienone, namely, 3,4-bis[4-(phenylethynyl)phenyl]-2,5-di(pyridin-2-yl)cyclopenta-2,4-dien-1-one. Analysis of the experimental results made it possible to modify the known synthesis procedure, which ensured a more than twofold increase in the yield of the desired compound.

The 2nd generation dendrimer with phenylacetylene groups at the periphery of the macromolecule was synthesized using a new tetraaryl-substituted pyridyl-containing cyclopentadienone. The dendrimer can be considered as potential ligand fragments for the formation of metal complexes and further nanoparticles. The purity and structure of the obtained dendrimer were confirmed by gel permeation chromatography, NMR spectroscopy, and MALDI-TOF mass spectrometry.

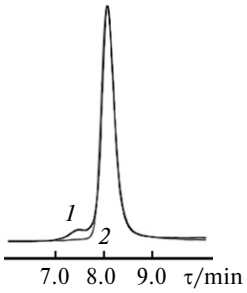


Fig. 2. Chromatograms of a mixture of dendrimers **8** and **8a** (*1*) and dendrimer **8** (*2*).

Experimental

^{1}H NMR spectra were registered using Bruker Avance 600 and Bruker Avance 400 spectrometers.

A C,H,N analyzer Carlo-Erba 1106 was used to confirm the elemental composition.

Mass spectrometric analysis was performed on a Bruker Biflex III MALDI-TOF mass spectrometer. *Trans*-indole-3-acrylic acid and sodium trifluoroacetate were used as a matrix and cationizing agent, respectively.

Analytical GPC was performed on a Shimadzu chromatograph using RID-20A and SPD-M20A detectors, and a Phenogel

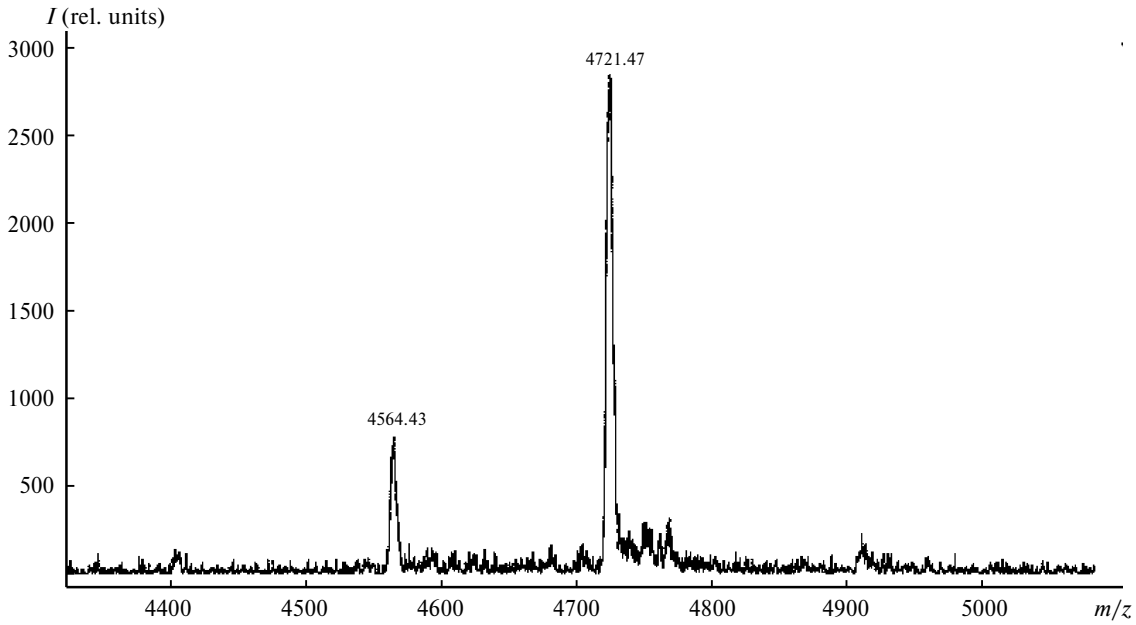


Fig. 3. MALDI-TOF mass spectrum of dendrimer **8**.

500A column (300×7.8 mm). THF was used as eluent, temperature was 40 °C, flow rate was 1 mL min^{-1}.

TLC was carried out using ALUGRAM SIL G/UV254 plates, carrier was silica gel 60 (0.2 mm) with fluorescent indicator (254 nm).

1,2-Bis[4-(phenylethynyl)phenyl]ethane-1,2-dione (3). A mixture of 1,2-bis(4-bromophenyl)ethane-1,2-dione (1) (0.500 g, 1.359 mmol), copper iodide (0.052 g, 0.272 mmol), triethylamine (2.5 mL), and toluene (0.75 mL) was charged into a Schlenk flask equipped with input for argon and a magnetic stirrer. Oxygen was removed from the reaction mixture by freezing in liquid nitrogen and double evacuation. Catalytic complex $Pd[P(C_6H_5)_3]_4$ (0.063 g, 0.543 mmol) was added to the mixture under an inert atmosphere. Then, repeated freezing and evacuation were carried out. A 10% excess of phenylacetylene (2) (0.4 mL, 0.305 g, 2.989 mmol) was added after thawing. The synthesis was carried out under an inert atmosphere at 80 °C for 1.5 h. The reaction was monitored by TLC, eluent was petroleum ether (5 mL), chloroform (2 mL). The reaction mixture was diluted with chloroform after cooling, then washed with a saturated solution of ammonium chloride until the blue color of the aqueous layer disappeared, then with 1N hydrochloric acid and distilled water to a neutral medium. The organic layer was dried over sodium sulfate with stirring for 5 h. The solvent was distilled off and the desired product was crystallized from chloroform. The product obtained in the form of a powder was dried in vacuum at 40 °C. The yield of product **3** was 0.501 g (90%). ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.39—7.40 (m, 6 H); 7.56—7.58 (dd, 4 H); 7.67 (d, 4 H, J = 8.3 Hz); 7.98 (d, 4 H, J = 8.3 Hz). T_m = 188—189 °C. Found (%): C, 85.09; H, 4.40. $C_{30}H_{18}O_2$. Calculated (%): C, 87.78; H, 4.42.

1,3-Dipyrid-2-yl-2-propanone (4). The synthesis of compound **4** was carried out according to described procedure.[6]

3,4-Bis[4-(phenylethynyl)phenyl]-2,5-di(pyridin-2-yl)cyclopenta-2,4-dien-1-one (6). A mixture of compound **3** (0.200 g, 0.486 mmol), compound **4** (0.125 g, 0.583 mmol, 20% excess), ethanol (2 mL), benzene (5 mL) was placed in a Schlenk flask equipped with an argon inlet and a magnetic stirrer. A catalytic amount of KOH (0.016 g in 2 mL of ethanol) was added dropwise to the reaction mixture with stirring and boiling over 3 h. The progress of the reaction was monitored by TLC (eluent was chloroform (1 mL), ethanol (0.1 mL)). At the end of the reaction, the precipitate was washed with cooled ethanol and dried at 50 °C *in vacuo* to constant weight. The yield of product **5** was 0.250 g (85%). ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 8.71 (d, 1 H, J = 4.1 Hz); 8.57 (d, 1 H, J = 4.1 Hz); 7.76 (t, 1 H, J = 7.7 Hz); 7.65 (t, 1 H, J = 7.7 Hz); 7.50—7.29 (m, 20 H), 4.18 (s, 1 H). Found (%): C, 85.36; N, 4.44; H, 4.65. $C_{43}H_{28}N_2O_2$. Calculated (%): C, 85.41; H, 4.67; N, 4.63.

To obtain the diene form of cyclopentadienone **6**, compound **5** (0.4 g) in ethylene glycol (15 mL) was heated to 165 °C and kept at this temperature under stirring for 30 min. The precipitate was filtered off, washed with ethanol, and dried *in vacuo* at 50 °C. The yield of compound **6** was 0.348 g (90%).

^{1}H NMR ($CDCl_3$, 600 MHz), δ: 8.58 (br.s, 2 H); 7.70—7.00 (m, 24 H).

Synthesis of the 1st generation dendrimer (compound 7). The 1st generation dendrimer **7** was synthesized based on 1,3,5-triethinylbenzene by the Diels—Alder reaction according to the previously described procedure.[14]

Synthesis of the 2nd generation dendrimer (compound 8). A mixture of compound **5** (0.397 g, 0.657 mmol), diphenyl ether (2 mL), and *o*-xylene (0.5 mL) was placed in a Schlenk flask equipped with an argon inlet and a magnetic stirrer. The mixture was heated to 130 °C, then a solution of the ethynyl-containing 1st generation dendrimer **7** (0.100 g, 0.073 mmol) in diphenyl ether (1.5 mL) was slowly added with vigorous stirring. The reaction was carried out at 170 °C for 9.5 h. After cooling, the reaction mixture was precipitated in hexane, the resulting precipitate was washed with hot ethanol until the excess of monomer was washed out (control by TLC, eluent chloroform (1 mL), ethanol (0.1 mL)), and dried at 60 °C *in vacuo* to constant weight. The

yield of the reaction product was 0.249 g (72%), the purity determined using GPC was 100%. ^{1}H NMR (CD_2Cl_2, 400 MHz), δ: 8.59 (d, 9 H); 8.25 (d, 6 H); 8.02 (br.s, 3 H); 7.63—6.51 (m, 198 H). ^{13}C NMR{^{1}H} JMOD (CD_2Cl_2, 125 MHz) δ: 89.58 (s, $C_{alkynyl}$); 89.62 (s, $C_{alkynyl}$); 89.80 (s, $C_{alkynyl}$); 120.70 (s, C_{quat}); 120.73 (s, C_{quat}); 121.16 (s, C_{quat}); 121.41 (s, CH); 121.49 (s, CH); 121.62 (s, CH); 121.81 (s, CH); 123.52 (s, C_{quat}); 125.40 (s, CH); 125.60 (s, CH); 126.72 (s, CH); 126.78 (s, CH); 127.08 (s, CH); 128.37 (s, CH); 128.64 (s, CH); 128.67 (s, CH); 128.76 (s, CH); 128.82 (s, CH); 129.70 (s, CH); 130.29 (s, CH); 130.31 (s, CH); 130.79 (s, CH); 131.31 (s, CH); 131.72 (s, CH); 131.81 (s, CH); 131.83 (s, CH); 131.92 (s, CH); 134.97 (s, CH); 135.18 (s, CH); 135.31 (s, CH); 135.57 (s, CH); 138.14 (s, C_{quat}); 138.22 (s, C_{quat}); 138.39 (s, C_{quat}); 138.56 (s, C_{quat}); 138.64 (s, C_{quat}); 138.73 (s, C_{quat}); 138.79 (s, C_{quat}); 139.79 (s, C_{quat}); 139.90 (s, C_{quat}); 139.96 (s, C_{quat}); 140.28 (s, C_{quat}); 140.42 (s, C_{quat}); 140.49 (s, C_{quat}); 140.54 (s, C_{quat}); 140.56 (s, C_{quat}); 140.87 (s, C_{quat}); 140.92 (s, C_{quat}); 140.99 (s, C_{quat}); 141.03 (s, C_{quat}); 141.19 (s, C_{quat}); 148.61 (s, NCH); 149.26 (s, NCH); 149.59 (s, NCH); 158.95 (s, N$\underline{C}$C); 159.26 (s, N$\underline{C}$C); 159.38 (s, N$\underline{C}$C); 159.77 (s, N$\underline{C}$C). MALDI-ToF MS, Found: *m/z* 4724 $[M]^+$. Calculated: M = 4722.

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